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UNIVERSITY OF TORONTO MEDICAL JOURNAL

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MARCH 1959

VOLUME XXXVI NUMBER 5

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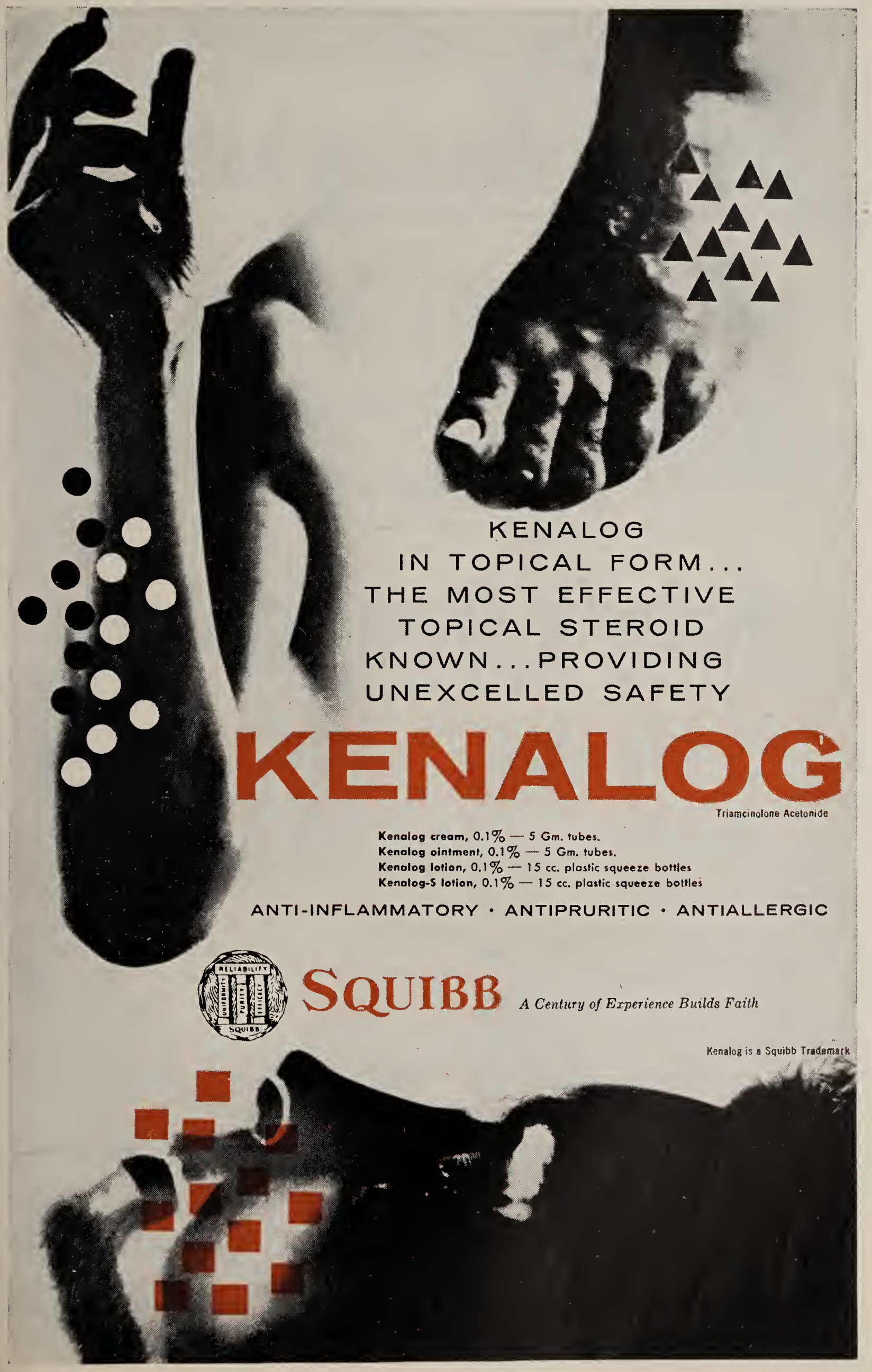
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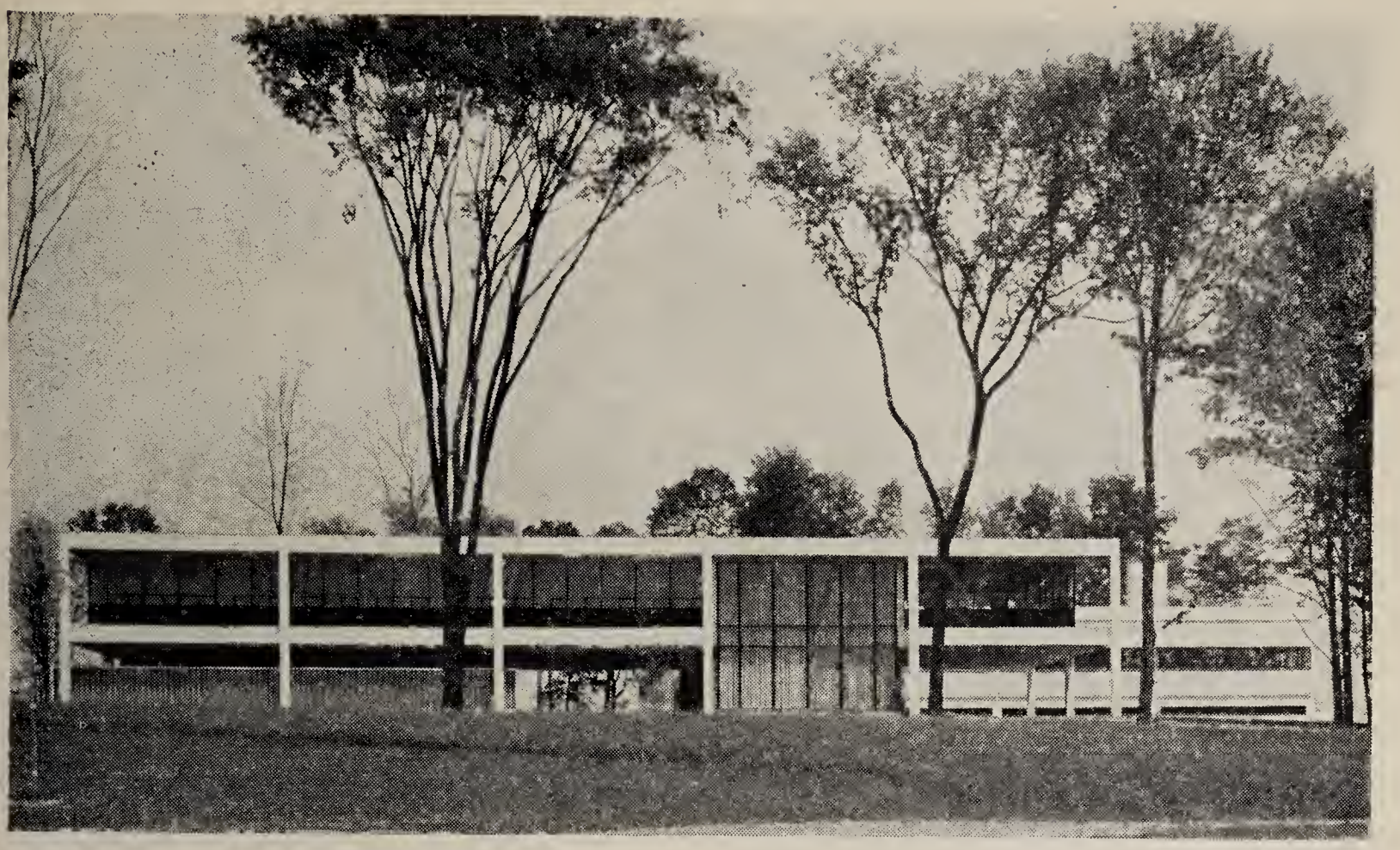

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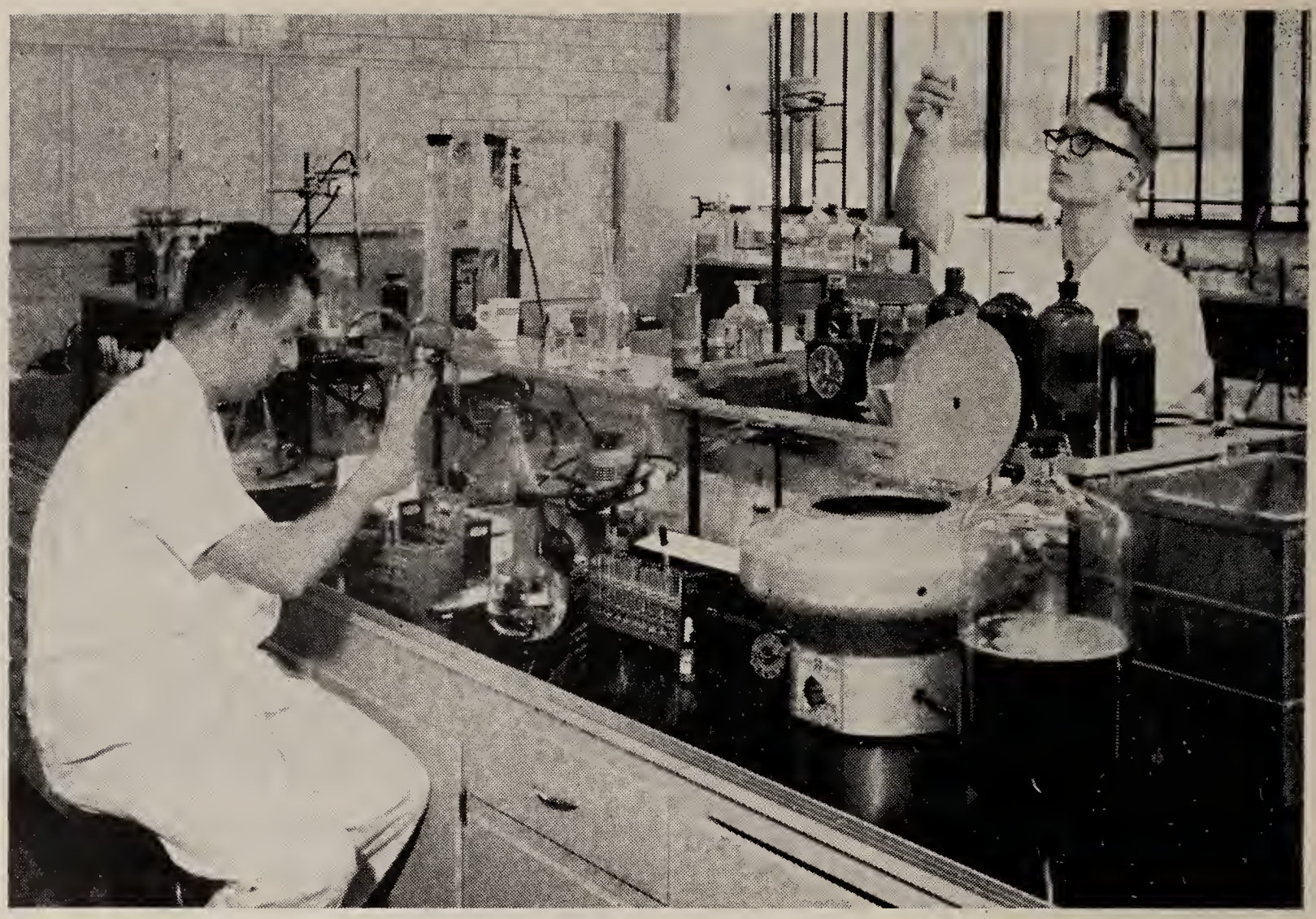

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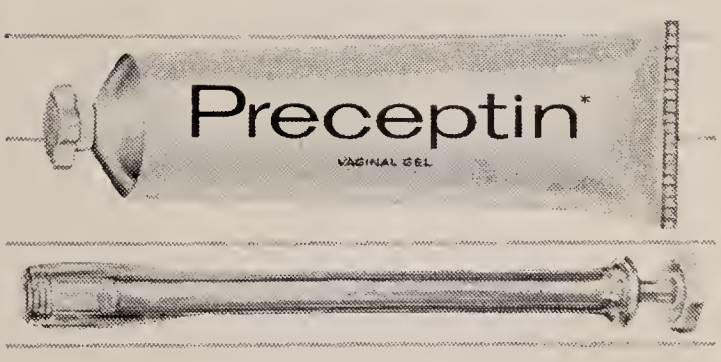

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ACUTE LEUKEMIA—Nature of the Disease

ANDREW BECKER, 5T9

Definition

LEUKEMIA, a disease of unknown etiology, is characterized by:

(1) an abnormal and widespread *proliferation* of the white blood corpuscles and their precursors; and

(2) the *infiltration* by these cells into the various tissues of the body, especially the bone marrow, spleen, liver, and lymph nodes.

In acute leukemia, the pathologic cell, in its morphology and speed of mitosis, shows various degrees of relative ontogenic immaturity; and its potential for infiltration, in terms of rapidity and extent, is a relatively great one. Clinically, leukemias are invariably fatal. It is the length of their spontaneous course toward such ending which determines whether they shall be called acute, subacute, or chronic. Acute leukemia has been arbitrarily defined as having a spontaneous clinical course of six months or less from the inception of symptomatology. It is conceded however, that the fatal termination of a leukemic disease obviously acute at the outset can, by current therapy, be deferred beyond these arbitrary limits. In other words, the diagnosis "acute" need not be made in retrospect. With few exceptions, there is general agreement that the leukemic state is neoplastic in its nature.

Epidemiology

1. FREQUENCY AND AGE. Deaths from leukemia represent approximately 4% of all deaths due to cancer. 30 to 35% of all leukemias are of the acute variety. Acute leukemia—which can be encountered at any age—is most frequently seen in persons younger than 20 years and has its greatest incidence in children under 5. At the Toronto Hospital for Sick Children, where malignancy is the commonest cause of death in children over 2 years of age, acute leukemia is the most common pediatric cancer, accounting for approximately ⅓ of all malignant tumors. Congenital leukemia (leukemia at birth) is a rare but authentic clinical entity.

Although until the age of 20 the great majority of leukemias are acute, not all cases of early childhood are acute, just as not all cases of leukemia in adults are chronic, though in adults, the latter is by far the commoner. Monocytic leukemia, which is more often acute than chronic, favors middle age. Furthermore, the protracted clinical finale of a chronic leukemia can be and is, not uncommonly, telescoped into one of relatively short duration by a sudden and intractable change into the acute form (blast transformation of chronic leukemia).

2. SEX. Acute leukemia shows a slight, statistically significant, unexplained male predominance.

3. RACE. There exists a significant lower incidence in Negroes. In the limited area of New York City, the Jewish population shows a higher leukema incidence rate than the non-Jewish part.

4. HEREDITY. Although the mode of inheritance is poorly understood, cases of acute leukemia developing more than once in a family have been reported. The probability that this should happen is very small, but the occurrence of a rare disease in several members of a family cannot be due to chance alone.

The association of acute leukemia with mongolian idiocy is a rare but well-documented pediatric entity.

Etiological Considerations

The etiology of leukemia is unknown, but a great deal of investigation, both

clinical and laboratorical, has attempted (with varying degrees of success) to unmask so-called *leukemogenic factors*. As a result, fascinating and doubtlessly important hypotheses as to the overall nature of the disease have been advanced.

A. CLINICAL LEUKEMIA

1. *Infection.* Infections of many kinds are common accompaniments of leukemia, although at present there are few students of the disease who would accept infection, in the common connotation of the word, as its cause. Bacterial infections may play a subordinate part in leukemogenesis, for leukemic changes in hematopoietic organs may remain quiescent (asymptomatic) for months or years until a superimposed infection suddenly makes obvious the presence of an underlying blood dyscrasia. Whatever the subsidiary function of bacteria, we cannot glibly dismiss—we presently shall see—the possibility of viral agents playing a primary role in the etiology of this disease.

2. *Neoplastic theories* are today the most widely accepted "explanations" for the leukemic processes. These theories derive their finest credentials from both cytopathological and clinical considerations, i.e., the malignant morphology and behaviour of the leukemic cell, and the relentless and invariably fatal clinical course. While such phenomena seem to exist in the case of acute leukemia, the neoplastic theories have been challenged by recent emphases on the relatively non-destructive, seemingly symbiotic behaviour of certain chronic forms of the disease.

3. *Chemicals.* Although absolute clarification of its role has yet to be forthcoming, *benzol* (in chronic poisoning) is the only chemical that at this moment can raise a reasonable claim to the status of a leukemogen.

4. *Trauma*, especially contusion of the abdomen or fracture of a bone, has resulted in the development of leukemia (usually of the myelocytic variety); but there is no conclusive evidence that such occurrences are not merely aggravations and expositions of latent or pre-existing subclinical forms.

5. *Ionizing radiation.* As opposed to the doubt concerning the etiologic significance of the above-mentioned factors, ionizing radiation has been shown beyond question to be leukemogenic. For leukemia has had a statistically significant increased incidence among physicians, radiologists, and among patients with ankylosing spondylitis who had received repeated therapeutic X-irradiation to their spines. Incidence studies of leukemia occurring among survivors of the nuclear blasts at Hiroshima and Nagasaki have further substantiated the concept of ionizing rays as leukemogens. Since it has been shown that the incidence of leukemia was proportional to the proximity of the survivors from the hypocentre of explosion; and similarly that in the therapeutic X-irradiation of Marie-Strumpell spondylitis patients, the larger the total accumulated X-ray dose the greater the chance of subsequent leukemia, considerable experimentation has attempted to determine whether the genesis of leukemic disease by means of ionizing rays depends upon the "accumulation" in the body cells of at least a *threshold dose of units radiation* or whether *any amount of radiation* (however small) contributes towards the development of this disease. A moment's reflection will make obvious the significance of such considerations in terms of preventive medicine. The above question, and others like it, have yet to be finally answered.

6. *Hormones.* There is evidence in some strains of mice that (1) estrogenic hormones are leukemogens, and that (2)

the incidence of leukemias so induced can be lessened by ovariectomy. These observations together with the fact that in humans most leukemias show a sex (male) predominance, lend support to the hypothesis that in some hitherto obscure way sex hormones (perhaps as "carcinogens") may be of etiologic import in the disease.

7. *Host Resistance.* A less evident, though very valid, approach to the problem of etiology concentrates on the so-called host-resistance factors. It is not inconceivable that imbalances (deficiencies or excesses) of factors controlling hematopoietic equilibrium could lead to a failure of normal, ordered, teleologically restrained leucocyte production or elimination, as resulting in qualitative and quantitative aberrations in the leucocytes. The fact that there exist physiologic differences between children and adults (though there is considerable overlap), and that there exist clearly delineated differences between the types of leukemia that affect children and adults (again, an overlap) —seems to point up the significance of host-resistance factors in the genesis of the leukemic process.

B. EXPERIMENTAL LEUKEMIA

Extensive studies on experimental animals have demonstrated the possible role of *filtrable virus bodies* in the etiology of leukemia.

There is no doubt whatever that viruses cause diverse kinds of leukemia in fowl and other birds (avian leukoses), and recently several of these viruses have been visualized in electron microscopic studies.

Attempts to ascribe a similar etiology to mammalian forms of the disease have in the past few years been crowned with considerable success. There has accumulated evidence that points definitely to the presence of self-propagating filter-passing agents as causative factors in the production of some mouse leukemias. The following are some of the important observed facts:

(1) It has been possible, by selective breeding, to develop strains of mice which have a very high incidence of spontaneously developing leukemia.

(2) Leukemic tumor cells from members of these high-incidence strains can be transplanted to members of genetically closely related strains with a very low incidence of spontaneously developing leukemia. A leukemia will result in the recipient animal, and this leukemia can be propagated within the low-incidence strain by continuous tumor-cell transplants to other members of that strain.

(3) Cell-free extracts from leukemic tumors obtained from high-incidence strain members, when inoculated into baby mice of low-incidence strains within a few hours after birth can result in the appearance of leukemia in the inoculated mice, but only after intervals of 5 to 14 months. During the latent periods, the inoculated animals live in apparently normal health.

(4) The same results as in (3) can be attained by using cell-free extracts from normal embryos of high-incidence strains as the inoculum, suggesting a *transmission of leukemogenic virus bodies from normal parent to normal embryo* within high-incidence strains.

As a result of such studies, Gross has proposed the hypothesis of the *Vertical Transmission of Leukemia.* Accordingly, viruses can be transmitted in an inactive form from one generation to another directly through the germinal cells causing only occasional symptoms of the disease. The virus agents in most cases and for long periods of time are perfect parasites causing no harm to the host. Now and then, for various outwardly nonspecific reasons (leukemogenic factors) or for no obvious reason at all,

the malignant potentialities of these agents become manifest. The result is leukemic disease.

Because it proposes to explain the hereditary component of leukemia, this hypothesis is at once bound to be attractive. And in this instance, the question of whether the nature of leukemia is neoplastic or infectious is meaningless, for such an hypothesis is nothing short of an explanation of neoplasticity. However, until a human counterpart of such phenomena can be more obviously demonstrated—and this may be impossible because of the immensely long latent periods involved—such an explanation cannot be considered to approach unequivocal finality.

Pathology of the leukemic cell

A. morphologic considerations

The nature of the abnormal leukemic cell has been used as a basis for micropathologic classifications of the acute leukemias. Any given form of the disease can be "pigeon-holed" according to the predominating cell type. Thus, if the leukemic cell has origin in the bone marrow, the leukemia is a myelogenous one; and if the origin of the abnormal cell is extramedullary, the leukemia is a histiocytic one. Further subdivision based on cellular morphology can be attempted as follows:

I. MYELOGENOUS

(a) *Myeloblastic (Granuloblastic)*
  (i) neutrophiloblasts or neutrophilic promyelocytes
  (ii) basophiloblasts or basophilic promyelocytes
  (iii) eosinophilic myelocytes

(b) *Myelo-monocytic (Myelo-monoblastic)*
  (i) myelo-monoblasts or myelo-promonocytes

II. HISTIOCYTIC

(a) *Lymphoblastic* (not considered myelogenous but may have intramedullary origin)
  (i) *Lymphoblasts*

(b) *Histio-monocytic*
  (i) histio-monoblasts or histio-promonocytes

(c) *Lymphosarcoma cell*

(d) *Plasma cell*
  (i) plasmoblasts or proplasmocytes

III. MIXED TYPES

Such classifications are generally considered unsatisfactory for several reasons. The division of the leukemias into myelogenous and histiocytic is vulnerable from the viewpoint that lymphocytes, plasma cells, and basophils can either be of intra- or extra-medullary origin. Frequently, due to its structural abnormality and extreme immaturity, microscopic differentiation of the leukemic cell into the correct subtype is difficult if not completely impossible; a diagnosis of *stem cell, hemocytoblastic,* or *blast cell leukemia* is then resorted to. It has been stated that such difficulties render the diagnoses of cell type too unreliable for conclusions to be drawn from them. Furthermore, with present forms of treatment, little is to be gained by such differentiation. And lastly, the labelling of a leukemic cell as a precursor of a specific leucocyte series (i.e., eosinophiloblast) tends to slight the fundamental concept that such a cell is in no real sense a precursor, but rather one so markedly altered in morphology and behaviour that it inevitably leads to the destruction of the host.

Pursuing this last point, we may state that the *cellular changes in acute leukemia favor the neoplastic hypotheses.* The nucleus/cytoplasm ratio is increased; there exist abnormalities in the size and number of the nucleoli; and

the patterns of mitosis are obviously bizzare. Electron microscopy has revealed curious fibrillar formations in the nucleus and cytoplasm typical for leukemic cells but never encountered in normal leucocytes.

B. DYNAMIC CONSIDERATIONS

The abnormalities in the behaviour of our leukemic cell appear to have an intrinsic basis—that of complex intracellular enzymatic and metabolic aberrations. The pathologic cell appears to be *fixed* in its relentless progressive evolution and in its ultimate lack of susceptibility to normal controlling mechanisms. And yet, it is capable of demonstrating sufficient *variability of behaviour* to render the clinical course completely unpredictable and inexplicable.

The disease can begin *de novo* or can represent the terminal stage of chronic leukemia or polycythemia. It is presumably characterized by an *incubatory stage* of variable and usually unknown duration consisting of minimal peripheral blood signs of marrow pan-insufficiency, and, on puncture examination, only slight bone marrow hyper- or hypoplasia without anything to suggest an impending leukemia. Such a stage usually goes unrecognized, or if discovered and diagnosed as such, is found to be totally resistant to known therapy.

Then a sudden change occurs. The marrow is replaced by sheets of leukemic cells which *invade the peripheral blood* in recurrent floods, and *infiltrate the various organs* (liver, spleen, lymph nodes, skin, mucous membranes, respiratory system, gastrointestinal tract, genitourinary system, bone cortex and joints, eyes, ears, nervous tissue, etc.) where they may manifest themselves by interference with local normal structure and physiologic function.

The leukemic process involves the rapid formation and destruction of large quantities of living tissue, with consequent *increase in protein metabolic turnover* and a resultant *elevation of oxygen consumption.* These phenomena manifest themselves clinically by the signs of *cardiovascular hyperkinesis* (tachycardia, peripheral vasodilatation, etc.).

Partial or complete remissions can occur either spontaneously or as a result of various types of therapy, but the inevitable outcome betrays the highly malignant nature of the disease.

PATHOLOGY OF THE BLOOD AS A WHOLE

Leukemia is associated with *changes in the blood plasma.* These include the presence of hypoalbuminemia, hyperglobulinemia, cryoglobulinemia, and other plasma protein abnormalities. In addition, changes in plasma enzyme systems are chemically detectable.

By the time most leukemic patients are examined, *anemia* of various degrees of severity is found. Most often the anemia is normocytic but it may be macrocytic. Normoblasts and polychromatophilic erythrocytes are usually present in the blood. The mechanism of anemia production in the leukemias is somewhat obscure. *Myelophthisis*, with "squeezing out" of marrow erythropoietic elements—or alternatively, with competitive consumption of blood "building blocks"—by infiltrating sheets of leukemic cells, has commonly been implicated. Recent investigations offer evidence for normal or increased marrow erythropoietic activity plus an *elevated erythrocyte destruction rate.* Demonstrable hemosiderosis and an increase in other products of red cell destruction in the urine and stool, as well as a demonstration by radio-isotopic studies that erythrocyte half-survival times are often as low as 50% of normal—tend to lower the stature of the myelophthisic hypothesis. Compromising, we might venture to state that myelophthisic activity might render the red cells susceptible to early, rapid destruction.

Thrombocytopenia is a very consistent finding and has been traditionally impli-

cated as the cause of *leukemic hemorrhagic phenomena*. The critical "hemorrhaging level" of platelets has usually been stated as 60,000/cu. mm. It is now known that there is no constant relationship between platelet count and amount or incidence of bleeding in leukemics. Some patients with normal or elevated counts may bleed, while others with very low counts may not. The abnormal thromboplastin generation which can often be demonstrated suggests the presence and role of *qualitatively defective platelets.*

Most leukemias at some stage in the disease will feature varying degrees of *leucocytosis.* Though leucocytosis is traditionally included among the most salient features of the leukemic syndrome, it has been treated with an intentional lack of emphasis in this paper. The reason is that leucocytosis is never demonstrable in some 10 to 20% of all acute leukemias, the condition being known as *aleukemic* or *subleukemic leukemia.* In fact, leucocyte levels in the peripheral blood are not infrequently less than the normal. In cases which do feature a leucocytosis, *aleukemic* or *subleukemic* phases are quite common. It is therefore imperative that if the syndrome of (1) normal or low W.B.C. (2) anemia (3) thrombocytopenia be discovered, the diagnosis of leukemia—and especially of acute leukemia—should be seriously considered and attempts to exclude it should be made. The finding of *abnormal immature leucocyte forms* in the peripheral blood is the laboratory sign which "clinches" the diagnosis.

Summary

(1) An attempt has been made to review the disease of acute leukemia from the viewpoint of current concepts regarding its dynamic nature.

(2) Since a consideration of pathogenesis without reference to clinical aspects is both difficult and undesirable, some mention of the clinical evolution of acute leukemia (without details of signs and symptoms) is to be found among the contents of this review.

(3) The proportionally large amount of space devoted to considerations of possible etiology mirrors the extent of literarily recorded speculation and experimentation on this most fundamental problem.

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METHODS OF TREATMENT IN PSYCHIATRY

J. C. STEELE, 5T9

"Our remedies oft in ourselves do Lie,
which we ascribe to Heaven"
—Shakespeare.

Object

IN the following pages, the author will briefly review contemporary methods of psychiatric therapy indicating the chief features of each. Space prohibits an adequate evaluation of individual techniques and thus this phase is only superficially dealt with. It is also beyond the scope of this paper to provide an "approach to the patient" for in no other field of Medicine do individual circumstances

and the clinical acumen of the therapist so influence the selection and application of therapy.

Pharmacological, physical, psychotherapeutic and environmental methods are distinguished.

I. Chemotherapy

Recent advances in this sphere have radically altered concepts of treatment, management and prognosis in the functional diseases. Psychopharmacological drugs may be assigned to one of three groups:

1. inhibitory

(a) *Cerebral Depressants*

This group includes the familiar sedatives and hypnotics (e.g. alcohol, barbiturate compounds, halogenated alcohols, etc.). Ease of administration, moderate cost, low incidence of side effects and the favourable response of many patients has led to their widespread use as control therapy in mild tension states and anxiety reactions. Tolerance, dependence, and addiction are frequent complications, but the incidence of these is reduced when availability is supervised and sedation is used selectively and as an adjunct to psychotherapy. Not uncommonly drugs of this group may, by selective depressive action, produce a state of heightened activity. This phenomenon is referred to as pseudo stimulation.

(b) *Ataraxics* (tranquillizers, neuroleptics, happiness pill)

This group has gained wide acceptance in clinical practice during the past five years. Ataraxics, meaning 'without perturbance', affect primarily subcortical centres without the undesirable impairment of intellectual function accompanying the cerebral depressants.

Classification

According to their chemical structure ataraxics may be classified in the following four groups: (See Table 1.)

(1) Phenothiazine derivatives
(2) Reserpine and related alkaloids
(3) Diphenylmethane derivatives
(4) Propanediols

Mode of Action

Despite intensive research programmes the exact mode of action remains obscure. Berger[1] divides the ataraxics into two categories:

(1) The autonomic suppressors include the phenothiazine, reserpine and diphenylmethane derivatives. It is postulated that they act:

(i) by stimulation of hypothalamic centres.[1]

(ii) by inhibition of the reticular activating substance resulting in diminished cortical arousal to sensory stimulation.[2]

(iii) by blocking central regulatory mechanisms which integrate autonomic and somatic functions.[3]

(2) The central relaxants include the propanediol derivatives. They do not affect autonomic function but produce a selective blocking of interneuronal circuits in the thalamic nuclei and exert a marked relaxant effect on spastic muscle. "Meprobamate . . . does not affect the hypothalamic regulating centres or normal responsiveness to stimulation, but it selectively reduces exaggerated responses."[1]

Side Effects

The administration of the autonomic suppressors may produce autonomic dysfunction, manifested by hypo- or hyperthermia, hypo- or hyperchlorhydria, constipation or diarrhea, postural hypotension, tachycardia, mucosal congestion and blurring of vision. Other untoward effects include parkinsonism (occurring in 10% of those receiving chlorpromazine), allergic skin reactions (8%), reversible regurgitation jaundice (occurring in 4%), agranulocytosis (0.1–0.02%), and convulsive seizures. Depression is an occasional complication of reserpine

TABLE I*

ATARAXICS

	Generic name	*Trade name*
1	Phenothiazine Derivatives	
	chlorpromazine	Largactil, Thorazine
	perphenazine	Trilafon
	proclorperazine	Stemetil
	trifluprомazine	Vesprin
	promazine	Sparine
	mepazine	Pacatal
	trifluperazine	Stelazine
	levomepromazine	Nozinan
	thiopropazate	Dartal
	acepromazine	Plegicil
	promethazine	Phenergan
2	Rauwolfia Alkaloids	
	reserpine	Serpasil
	deserpidine	Harmonyl
	rescinnamine	Moderil
3	Diphenylmethane Derivatives	
	benactyzine	Suavitil, Levol
	hydroxyzine	Atarax
	phenyltoloxamine	PRN
	azacyclonol	Frenquel
4	Propanediols	
	meprobamate	Miltown, Equanil, Trelmar
	phenaglycodol	Acalo

*Adopted from the Canad. M.A.J., Nov. 1, 1958, vol. 79.

medication. These toxic effects by and large are readily controlled by specific therapy, by dosage adjustment and by the substitution of another derivative.

The chief side effects noted with the propanediols are dermal hypersensitivity reactions, acute nonthrombocytopenic purpura and physical dependence with withdrawal symptoms.

Indications

(1) Autonomic suppressors are used largely in psychotic states for—

(i) symptomatic sedation

(ii) the treatment of acute exacerbations

(iii) the maintenance of remission

(2) Central relaxants are indicated in the management of acute psychoneurotic states associated with agitation, tension and anxiety, as an adjunct to psychotherapy.

Estimate

A summation of the literature indicates that two-thirds of all psychotic patients are moderately to markedly improved on tranquillizer drugs. Acute states associated with emotional agitation and behavioural disorder respond more favourably than do chronic regressed states. In mental hospitals continuous baths and isolation cells have been rendered virtually obsolete. Many custodial patients have returned home on maintenance medication and others allowed more limited freedom. Improved behaviour has created a need for more extensive psychiatric and social programmes.

The propanediols are effective in the treatment of tension states. The attention given this group of 'happiness pills' accounts for their popular prescription. It has been said of meprobamate that

"it is a good deal less honest than whisky and a good deal more expensive than phenobarb." "In the field of neurosis, tranquillizers have proved a dramatic failure in accomplishing what was and still is claimed for them by their manufacturers."[5]

Philosophers protest these psychophysiological panaceae. It remains doubtful, moreover, despite their widespread use, that "human beings will be able to achieve effortlessly what in the past could be only achieved with difficulty, by means of self control and spiritual exercise."[4]

2. EXCITATORY

Xanthine derivatives (e.g. caffeine) and amphetamine are familiar centrally acting stimulants. More recent drugs showing similar activity are pipradrol (Meratran), methylphenidyl (Ritalin), iproniazid (Marsilid), and deanol (Deaner).

Indications for their administration include—

(a) mild neurotic depression associated with lassitude, insomnia and/or apathy,

(b) moderate to severe neurotic depression. Hypnotics are administered concurrently to counteract the tension heightening effect of the excitatory drugs,

(c) psychotic depressions where ECT is medically contraindicated or the patient (or his family) refuses consent. Favourable response to imipramine (Tofranil),[2] and dextro amphetamine in combination with chlorpromazine[6] has recently been reported,

(d) lassitude occurring during treatment with derivatives of the automatic suppressor group where continued medication is required.

Anorexia, flatulence, palpitations, hypertension, insomnia and restlessness are relieved by adjustment of the dosage.

3. PSYCHOTOMIMETIC

Mescaline and lysergic acid diethylamide (LSD) which are known to induce a self limited, experimental schizophrenic type psychosis have been used as an aid to abreaction in psychotherapy.

II. Physical Methods

1. ECT, EST, ELECTROPLEXY

Electro convulsive therapy is an empirical technique first used by Cerletti and Bini in 1937 as a modification of von Meduna's chemoconvulsive method developed in 1934 from the (dubious) observation that epilepsy was rarely encountered in schizophrenia.

The modus operandi remains obscure. Both psychology and physiological factors are operational. Most workers feel the latter predominate with the selective impairment of cerebral centres secondary to a transient anoxia. Roth, in 1952, demonstrated EEG changes in the diencephalon following ECT.

The technique is relatively simple, the facilities required minimal, the contraindications few (if the psychiatric condition warrants), the complications rare, and the response (among correctly selected patients) dramatic. Such a happy therapeutic combination has led to the frequent abuse of this mode of therapy from the improper selection of candidates.

The patient is prepared with light diet and atropine. He is placed on a padded bed with a mouth guard and attendants to restrain him during the clonic phase. A grand mal seizure is induced by electrodes placed on the temples and the passage of a current of 70 to 130 volts for 0.2 to 0.5 seconds, dependent on the patient's threshold. Treatments are performed two to three times a week for a total of 10 to 25 seizures. If response is likely, improvement should be noted after four to six seizures.

Refinements include the preconvulsive administration of light intravenous anaesthesia, muscle relaxants, and oxygen. These methods allay the patient's apprehension and reduce the incidence of fracture-dislocation. Other complications include prolonged apnea, transient memory loss, which may persist up to three months, and, rarely, aspiration pneumonia.

Cerebral arterial sclerosis, extensive myocardial damage, and active tuberculosis are absolute contraindications.

ECT is used chiefly in the treatment of psychotic depressions (i.e. manic depressive depression and involutional melancholia). Reactive, psychoneurotic, depressions are frequently aggravated.

2. ICT, INSULIN COMA

In 1933 Sakel, of Vienna, reported his use of iatrogenic hypoglycemia in the treatment of schizophrenic psychosis. The technique has gained universal acceptance and its basic features have persisted unchanged.

The more complex and phylogenetically more recent areas of the forebrain are "metabolically more sensitive" than those of the lower brain stem and, in consequence, affected first during hypoglycemia.

Contraindications vary with the experience and enthusiasm of the therapist. It is generally accepted that the patient should be between 16 and 45 and without serious coexisting organic disease.

Sakel describes four phases in ICT.

Phase 1: 20 units of insulin are administered q.7 a.m. with daily increments of 5 to 10 units until a dose is obtained which produces coma.

Phase 2 dates from the first coma. Coma should not appear until the third hour after insulin administration and should not be prolonged more than 1.5 hours. (The duration will vary according to the depth of coma and the patient may be aroused with intravenous or gavage tea and sugar solution.)

Phase 3 denotes the seventh day of the week when patients are allowed to rest.

Phase 4 is the rapid reduction of the insulin dosage to nil in the course of a few days.

Fifty hours of coma are considered the optimum but this is by no means absolute. If improvement continues, up to 100 hours of coma may be used. Indications for interruption of therapy include laryngospasm, tachycardia, cardiac irregularity, persistent hypertonus in extension, and epileptiform seizures in the pre-coma state. Complications include after-shock (hypoglycemia occurring twelve hours after recovery), allergic reactions, transitory nephritis, primary oliguria (which pituitrin administration rectifies), pulmonary edema, and aspiration pneumonia.

ICT is indicated in the treatment of schizophrenic disease with reactive features, of recent onset (less than three months), in younger persons with a "good" personality prior to illness.

3. PSYCHOSURGERY

For twenty years, surgical interruption of the frontothalamic radiation which extends between the dorsomedial nucleus of the thalamus (the physical substratum of emotion) and the frontal cortex has been employed widely in chronic functional conditions (chiefly paranoia, involutional melancholia, obsessional compulsive neurosis and schizophrenia (where a strong effective colouring is maintained) characterized by concern for self and by much subjective suffering. Candidates are selected on a basis of symptomatology rather than diagnosis.

Indications for prefrontal leucotomy include the aforementioned plus:

(a) a failure to respond to conserva-

tive therapy without hope of a spontaneous recovery,

(b) emotional disablement barring the patient from useful occupation and a modest enjoyment of life.

A favourable response, obtained in two-thirds of the patients, is reflected in a relief of tension, a restoration of energy and a reactivation of interest (one-third will make a social recovery, one-third will be improved, and one-third will remain unchanged). Results will be determined by the previous personality of the patient, his reaction type, and the extent and locus of the surgical cuts. Experiments in monkeys have shown their post-operative behaviour to be that of "good-natured drunks".

Complications include epileptiform seizures (10 to 15%) which are controlled by anticonvulsant therapy, and post-operative mortality (2%). Deterioration of behaviour and blunting of the personality are observed in a small percentage.

4. CONTINUOUS NARCOLEPSY

The spaced administration of hypnotics to maintain continuous sleep for twenty hours daily was originated by O. Woolf in 1901. It is used chiefly to shorten the duration of agitated psychotic reactions which would ultimately regress spontaneously (e.g. manic psychosis, agitated catatonic schizophrenia and severe reactive anxiety states). Focal sepsis is a frequent complication which must be anticipated. Since the advent of neureleptics it has largely been abandoned, for the recovery rate among patients so treated falls short of the spontaneous recovery rate.

III. PSYCHOTHERAPY

Psychotherapy is defined as the treatment of emotional and personality problems and disorders by psychological means. Individual needs will dictate where the patient will be treated (i.e., in hospital, clinic or office), the method of approach (i.e., individual or group techniques or both), and the goal of therapy (i.e., whether conservative palliative, supportive and non-exploratory or more radically investigative, insight uncovering and personality altering). Outlined below is a brief classification indicating the major psychotherapeutic approaches. This division is somewhat arbitrary and it is to be appreciated that in practice there is much intermingling and overlapping.

1. INDIVIDUAL TECHNIQUES

(a) Genetic Dynamic Therapies entail the re-examination and re-evaluation of intra- and extra-psychic disorders with the patient in an attempt to reconstruct and buttress his personality. These forms of therapy are frequently protracted (more than three months), subjectively distressing, and require skilled psychiatric personnel. They are primarily insight discovering methods. The patient must be intelligent, co-operative, and financially able to undergo a full course of treatment. Best results have been obtained among chronic psychoneurotics.

(1) Psychoanalysis

Freudians see the origins of neuroses as aberrations of response arising from conflictual experience in infancy and childhood. Presenting problems are related, by the exploration of the unconscious, to earlier subjectively significant experience in an attempt to demonstrate their genesis to the patient.

(2) Psychobiological

Adolph Meyer school, while recognizing early experience as significant, assumes that many deviations arise during the later stages of personality development. The patient consciously re-examines life situations and responses (distributive analysis) which relate to present patterns of behaviours and emotional responses. By inductive reasoning

and discussion with the therapist he utilizes the analytic information to constructively modify his personality traits (synthesis).

(b) Other Non-Exploratory Psychotherapeutic Techniques do not attempt to reveal the etiology of malfunction but tend to be superficial and supportive.

(1) Superficial Expressive Therapy

This is an exploration and expression of pre-conscious mental content. Ventilation provides an opportunity for "talking things out" in a therapeutic setting. Frequently the patient's formulation of hostility and resentment is sufficient to alleviate a threatening or crucial situation. Abreaction is the emotional expression of a repressed frustration producing desensitization in a specific psychological area. Narcosynthesis employs intravenous sodium amytal, pentothal and methedine as a chemical adjunct to induce a state of increased communicability and decreased emotional control in order to overcome resistance and inhibition to heighten suggestibility, and to establish a meaningful rapport.

(2) Suppressive Therapy

An attempt to encourage repression, strengthen existing healthy defense mechanisms, and lessen anxiety is made by the use of persuasion, suggestion, and reassurance. Persuasion seeks to buttress the flagging personality by intellectual explanations and moralizing discussions. Hypnosis is defined as "an induced associative state produced through suggestion". It is chiefly employed in the modification of immediate distressing symptoms which thereby permits a more comprehensive reconstruction of the personality.

(3) Supportive Therapy

Anxiety is relieved by reassurance, counselling, suggestion, reasoning, encouragement, and alteration of the environment in an attempt to maintain an adequate functioning adjustment.

2. GROUP TECHNIQUES

Group therapy is widely employed in conjunction with, or as an alternative to, individual psychotherapy. Small groups selected on a basis of diagnosis, cultural background and intelligence, meet as frequently as is dictated by the group's goals under the supervision of a trained therapist. The therapeutic advantages of group techniques are obvious, for this dynamic social group which reflects the collective needs of its individual members operates so as to allow expression and critical analysis, encouragement and competition in a therapeutic and protected setting. In short, members tend to help one another while being helped as a unit. In this setting, anxiety is diminished, and "transference" to the therapist modified. Thus the depth of insight may be less than that obtained in individual psychotherapy.

3. ACCESSORY ACTIVITIES

This field encompasses those methods man possesses "for occupying and diverting his mind, for enjoyment and for creative activity". Hospital care ideally offers a varied programme of occupational therapy intended to encourage and develop existing skills, and to demonstrate creative talents (e.g., manual, musical, artistic, literary, etc.). It also offers entertainment of a physical and mental nature (e.g., organized sports programmes, movies, T.V., dramatic productions, etc.). Such a programme if correctly supervised is both curative and prophylactic, for it diverts the patient's attention from his "sweating self", produces a return of self confidence and adds a stabilizing breadth to personality.

Activities similar to those outlined above and having the same aims are recommended, where applicable, for those treated on an out-patient basis.

IV. Environmental Hygiene

The patient must be treated in his environment. Successful rehabilitation will, therefore, frequently necessitate a modification of his or her socio-economic habitus. Recommendations will vary with the individual's circumstances.

Investigations should include a review and an evaluation by the therapist (or department of social work) of:

(a) the patient's dynamic life situation, with an estimate of its role in the etiology, prolongation, and aggravation of mental disease;

(b) the patient's response to and subjective views regarding his environmental situation;

(c) the desirability and/or feasibility of alteration. Major changes are commonly impractical, but frequently alterations of a minor nature will do much to alleviate tension-producing states. Advice and counselling may be given to the patient or family or employer by the psychiatrist or by workers in related fields.

Efforts to maintain and treat the patient in his environment and thus to avoid the necessity of hospitalization are reflected in increased out-patient facilities and day-care programmes.

Social workers are attached to most psychiatric clinics and play an important role in the supervision of the out-patient's environment and activities. Other governmental and voluntary community social agencies which may be utilized include:

(1) Counselling Services
(2) Health Services
(3) Recreation Services

The extent of these services will vary according to the needs and social conscience of the community.

Conclusion

In limited space I have attempted to present a superficial survey of the psychiatrist's kit bag. Such a condensation is characterized by many failings, chiefly those of generalization and abstraction. It is hoped, however, that it will provide a basis for expanded reading and clinical experience.

Acknowledgement

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ALCOHOLISM AND GENERAL PRACTICE

HUGH LITTLE, 5T9

Prologue

IN 1957, this journal published two articles relating to alcoholism; one dealt with etiology and the other with medical complications. The aim of this article is to discuss the long interval between parental rejection and oesophageal varices, and to suggest various ways to influence the natural course of the disease.

The world's concern over alcoholism, as with so many other social evils, has led to the creation of alcoholism specialists. The simple act of creating specialists seems to have absolved the average doctor from the feeling that he ought to work with this difficult group of patients. Very often the alcoholic is summarily dismissed with a referral to a psychiatrist, a clinic, or Alcoholics Anonymous.

The social conscience of the student, nurtured through years of "public health", may well cry out at such brusque treatment. However, the prevalence of this madness suggests that there might be method in it. After all, what can the General Practitioner do for an alcoholic? And, equally important, can inadequate or ill-advised therapy do the patient much harm?

The following is an attempt to answer these questions.

The Nature of the Disease:

A. E. Housman once wrote that,

"—malt does more than Milton can
To justify God's ways to man."

Most medical students will agree that alcohol, used as an occasional relaxant, can make the world look very warm and pleasant. Most of us will continue to be able to enjoy alcohol as a thirst-quencher, a condiment, or an acceptable social ritual. There will be a few of us, however, who will find alcohol becoming more than this. Alcohol can provide a temporary adjustment to painful psychological needs. This adjustment will bring many unwelcome problems, but, until the sequels are more unpleasant than the cause, the alcoholic will resent any interference with his pursuit of happiness.

The depth of these needs and the success of adjustment prior to alcohol will, to a great extent, determine the course of the illness. Some, called primary alcoholics, will show the complete picture within three or four years of the initial drink. The majority will drink for fifteen to twenty years before reaching their "lowest point", usually in their fifth decade.

There are as many opinions about the needs of the alcoholic as there are writers in the field. Freud and the psychoanalytic school suggest that the "pub" and the companionship of drinking men is the ideal spot for the sublimation of a repressed homosexuality. Abraham suggests that the close tie between alcoholic intoxication and sex is really an inverse relationship; as the sexual powers decrease with age, alcohol and the ability to consume it become a substitute. Another writer suggests that the guilt feelings, associated with the latent homosexuality of the alcoholic, result in a fear of castration and the drinking becomes a protective mechanism by which he regresses to a pre-genital state.

A psychologist suggests that the parent-child relationship, in which one parent controls by too much love (love-dominance), and the other rejects by too severe standards, will result in an emotionally stunted individual. When the age of maturity arrives and society demands adult behaviour, the first few attempts to meet these demands may

end in failure and frustration. If, during these attempts, the individual encounters alcohol, he may feel that this is the socially acceptable way to escape the pain of his social catastrophe. Social and environmental factors can have a profound influence on the development of alcoholism. Both the soldier and the Frenchman are liable to alcoholic habits because of the propinquity and social importance of their respective mess or bistro.

Seldon Bacon states that the alcoholic is characterized by: 1) continual psychological pain; 2) a set of responses that may be characterized as immature; 3) an overall attitude of extreme egocentricity. This pain is centred around his feelings of failure, his extreme sensitivity to criticism, often bordering on paranoia, and his fear of any new situation in which he may fail again. The immaturity is seen in his rapid mood swings, facile rationalizations, and adolescent self-consciousness. The alcoholic's interests are seldom broader than self—his fear, his failure, his increasingly solitary existence. The alcoholic has few "significant others". As the illness progresses, he withdraws farther away from all associations, becoming the source of his own stimulation and forfeiting any external check on his fantasy.

The alcoholic drinks compulsively. He takes too much. Then he begins to have blackouts. He finds it necessary to drink alone, to start the day with a drink, (morning withdrawal symptoms), and finally to go on the periodic binge. During this time he will try all sorts of stratagems to control his drinking and when these fail the frustration will lead to more drinking. As the physical symptoms appear, they too will be washed away, with a consequent tightening of the vicious circle.

When the alcoholic finally seeks help, he will be suffering on every level of his being. His problems will run the gamut of physical symptoms, psychic pain, debt, criminal action, impotence and family breakdown. He will want help but he will be very ambivalent about giving up any of his defences. Treatment will be difficult for him.

TREATMENT:

With such a generalized illness we must be prepared to offer aid on many levels. First we must try to remove the distressing physical symptoms of prolonged alcoholic intoxication. This aspect of treatment will probably get full co-operation, but co-operation may end here. Human beings resist efforts to change their lives, and rightly so. Thus, the prerequisite for any intensive therapy is the patient's acceptance of the existence of a problem and an active desire to get help.

The patient wants help with the immediate control of his desire for alcohol. He wants help with the underlying psychological problems that are causing him distress. The alcoholic who accepts his problem has a deep sense of failure. He wants to re-establish his sense of personal worth. He wants help in rebuilding his family and his place in society. Can the General Practitioner adequately give help on all these levels? I feel that the General Practitioner alone can do only a partial job, whereas a fully staffed clinic can offer skilled aid where it is needed.

Still, the clinics are few, the alcoholics are many, and the pressure on the General Practitioner is continuous. Therefore, when the patients asks for aid, the most sensible approach seems to be as follows:

(1) Make a diagnosis and impart it to the patient.
(2) Tell the patient about the available facilities for treatment. Refer but don't dismiss. The patient may not yet be ready for intensive therapy

and an injudicious dismissal may deprive him of a trusted contact when he is ready for help.

(3) Do not give sedatives or other substitute drugs except in a controlled situation.

The manner of imparting the diagnosis is a very significant step in treatment. All of us have an attitude towards alcohol usually a complex mixture of excitement, fear, and perhaps disgust. Whatever our attitude, the patient will sense it within five words. If we feel any moral superiority, or cannot adequately differentiate between drunkenness and the drinker, we can rest assured that the patient will not be looking for constructive help, if he returns. Our attitude is the most important single factor in the treatment of alcoholics—and the most difficult to manage.

Both doctor and patient may enter the initial interview with crippling preconceptions. The patient may see the doctor as the personification of middle class morality, one who will throw him out of the office with orders to come back after he's been sober for a month. The patient may approach this threat by aggression or grovelling. The doctor may see the patient as one of "those hopeless, spineless alcoholics who do nothing but borrow and drink". There can be no successful treatment unless some real communication can break through these boundaries.

The possible facilities for treatment can be classified as follows:

Site: (1) In-patient Institutional Care for selected cases
(2) Out-patient Clinic Care
(3) Alcoholics Anonymous or Salvation Army
(4) Family Agencies in smaller centres
(5) Psychiatric Consultation
(6) General Practitioner

Types of treatment:
(1) Medical
(2) Psychological: analysis
hypnosis
conditioned reflex
religious conversion
psychotherapy
(4) Supportive: multi-level
(3) Psycho-Social: group therapy
protective drugs

If, either by choice or necessity, the General Practitioner decides to treat an alcoholic, there are a few basic things he should remember.

It is best to think of alcoholism not as an abnormality of function to be restored to normal, but as an abnormality of development with which the alcoholic can function only by drawing on other strengths. Thus treatment is not aimed at restoring the alcoholic to the state where he can drink moderately. We must help the alcoholic use all his resources so that he can function *without alcohol.*

Most General Practitioners will not be ready to embark on heroic programmes to establish an alcohol-emetic reflex through the use of apomorphine. Few will attempt hypnosis. Perhaps even fewer will attempt religious conversion. However, because of the great need, some will try their hands at that peculiar form of teaching called psychotherapy. Combining this with help on socio-economic levels will probably get the best results.

Psychotherapy is teaching of the most delicate kind. It starts with the patient's fears around treatment. It must combine the facts about alcoholism with sympathetic understanding of his fears. It is an "art in which knowledge of the science of human relations, and skill in relationship, are used to mobilize the capacities in the individual and resources in the community appropriate for better adjustment between the client and all or any part of his total environment". The principles involved in effecting this

therapy are easy to list but difficult to apply. The only instrument we can use is ourselves.

We must respect the patient's need to be treated as an individual and not as a "case". We must realize that the patient has negative feelings, (fear, resentment and hate), and accept his ambivalence. We must accept the individual's need to be treated as a person of innate integrity, regardless of his all-too-obvious faults. If we are to help the patient we must give sympathy and a response to the feelings he expresses. The patient must be neither judged nor condemned for the difficulties in which he finds himself. The patient *must* make his own decisions. It is too easy for us to command, and it may be too easy for him to be commanded.

The difference between being "therapeutic" and being just "understanding" is often imperceptible, but it lies in the control exerted within the relationship. Thus, the expression of feelings should not be to "blow off steam", but to free the patient for positive action by seeing his emotions in perspective, and having his negative feelings accepted as normal by the doctor. The patient may try to manipulate the doctor to the position of having status invested in the patient's maintenance of sobriety; the "you're-doing-this-for-me" approach. This is dangerous because any negative feelings, either towards the doctor or the treatment, might result in a binge which would cause the doctor either to lose status or to reject the patient. We are a proud people and would be inclined towards rejection. This would allow the patient to return to his bottle with the rationalization that no one really cares. It is better to anticipate this test and explicitly accept the improbability of immediate success. The art comes in the judicious balance of emotional involvement.

Group therapy has many values. If the patient is accepted in the group he will begin to feel a return of personal worth. Identifying with a group whose aim is sobriety will add strength to the patient's own intent. This supportive aspect will be combined with the informal education that comes through comparing one's experiences with those of one's peers.

The protective drugs, Antabuse and Temposil, (citrated calcium carbimide), are valuable adjuncts to therapy. These drugs interfere with the oxidative enzymes which metabolize alcohol, resulting in a toxic accumulation of acetaldehyde. The subsequent distressing symptoms act as a deterrent to drinking. If the patient does choose to use these drugs, they will protect him from the impulsive drink. Thus he will have to make a break with treatment, conscious or not, before he can get his accustomed alcoholic release. The new drug, Temposil, works faster than Antabuse, gives less severe reactions, less side effects, and removes most of the physical contraindications to protective drug therapy.

The alcoholic cannot be frightened into sobriety by threats of a cirrhotic death, he is already frightened and he has found a solution for fright. To diagnose alcoholism, and recommend sobriety is one of the gravest responsibilities a doctor can assume. The alcoholic has relinquished friends, family, a job and even his self respect to maintain this defense. We must be prepared to offer him something pretty good or we are not doing him justice. The best we have is ourselves.

EPILOGUE:

This article is an attempt to spin a thread of fibres which are plucked from the works of others. The author cannot pretend that this thread is a strong cable, sufficient to secure our subject for

a long and hazardous trip through time. However, it is hoped that it will provide a sound fabric on which to base our dealings with the problem of alcoholism.

I would like to apologize to J. D. Armstrong, R. J. Gibbons, F. P. Biestek, and S. D. Bacon, whose respective works I have so severely plagiarized.

I would like to thank Dr. Stan Freeman who took time to correct the spelling as well as to add greatly to the content of this article.

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MEDICINE—MEANS OR END?

BERNARD SLATT, 5T9

IN any community where a doctor's service is required that service can best be rendered if the doctor has the technical skill and gracious art to ply his trade, and the credulity of the troubled flock who search his door. These two prerequisites are essential for both the disposal and uptake of therapy. For without ability, there remains only the affectation of the doctor figure, and without trust the patient places his life into the arms of chance. As one essential mutually contributes to the welfare of the other, so it can occur that one may parasite from the foundation of the other and so exist, but concurrently weaken the structure upon which they both rest. The doctor, with a cosmetic air of solemnity and omniscience, can easily fool the most informed of his clientele with the incantation and rites of medical ceremony and hide his deficiencies under a glossary of impressive but meaningless diagnoses, and flattering but useless prescription. His faculty for carrying out this ruse is augmented by the confidence harboured for the profession as a whole, of which he is an elective sample, and by the reticence of his fellows to reveal his shortcomings lest they sully the banner under which the entire company of practitioners march. At the other end of the seesaw, efficacious and considerate treatment by the doctor may be undermined by the suspicious, cynical patient whose belief in his powers is questioned because of previous unpleasant experiences or philosophical tenets which he holds, incompatible with medical dogma.

The task of building up the lay trust is carried by the individual doctor. If he utilizes his full knowledge and resources, makes precise diagnoses to the best of his ability, and ministers appropriate remedies to arrest disease and comfort the patient, he justifies his position. Anything which does not employ the complete complement of his talents, breaks with scientific etiquette as it increases the amount of guesswork. Moreover, it betrays that very confidence required to sustain a practice. Ironically enough, many ailments will either cure themselves or be arrested with buckshot therapy, and the slack doctor may enjoy a flourishing calling with little loss, except for the loss of self-respect and professional dignity.

Humbuggery works, but it is not to

be condoned. How is it to be exposed for its own worthlessness without doing damage to the general movement of medicine upon which sincerity and good will thrive? Outsiders, such as osteopaths, homeopaths, serum healers, bone setters and chiropractors are disclaimed as dissenters from the ranks of biology, physiology and therapeutics. Although they are not given formal recognition, they are not outlawed, for in medicine itself the query between myth and fact still remains and indeed, the staunch supporters of the purely scientific approach still blush because many daily practices are based upon empirical and pragmatic evidence. Unjustly or justly, the aliens are decimated by snobbishness. They are not allowed to join current societies, confer and consult on an equal footing with accredited practitioners, sign death certificates or recommend drugs. But the despoiler within the ranks, who is sheltered by the wing of public acceptance and medical ratification, is potentially a more noxious agent than the unorthodox healer. His freedom is unlimited, and as long as he does not overtly break medico-legal law, his errors are forgiven rather than challenged. With a bit of pedagogy, a few well-chosen phrases that might be heard in any sermon on a Sunday morning, and assisted by powerful allies in combating disease, namely spray drugs, nature and time, he can grope through the dim light of uncertainty, satisfying his clientele that he has helped them, and himself that he has done his job well. Sympathy doctors, though deluded by their own charms, can control in this way many of the minor ailments which accost them. However, they are a menace when they wax lusty and become commercial, unethical and place their duty to themselves before the patient. To expose them to the public is folly, to expose them to themselves is the only recourse.

The question which follows is, how does this fine fruit of the tree of medicine go sour? It does, and it is only hysterical focussing to say that it doesn't. However, because one apple in a barrel of apples is rotten, doesn't mean the rest are all rotten. It simply means that one rotten apple exists. To understand this process of fermentation, consider the prospect about to enter medicine, the change he undergoes there, and the resultant product upon whom is given the title of doctor. The high school graduate, before choosing medicine, scans the glitter of the various fields and endeavours to discover which course is commensurate with his own interests. At this stage, the tainted seed often begins to grow, for if the person's objectives are base, the training he receives will only serve to expedite those base motives. Maturation may eventually cancel some undesirable traits, just as growing up can destroy a young boy's glamorous ambitions. The medical school too exerts an influence just by providing an atmosphere of research, learning and recognition for meritorious work. These forces, plus innumerable gentler tides, such as good fellowship, professional pride, and inspiring subjects and professors, although they can modify or eclipse unhealthy preliminary motives and replace them with more stolid aims, can also fail in their attempts to refine the crude material which is fed into the stoker of pre-medical training. The emergent product, who enters medical school cravenly and leaves cravenly, unfortunately has the same galvanized exterior as his mates. He is an excellent counterfeit, and like many counterfeit articles, can deceive and escape detection except under the most scrupulous eye. As George Bernard Shaw remarked, "the superficial airs and graces are but the embroidery of quackery, and we could well afford to smile at them, were they not indicative of a more serious derangement within".

To descend from the general to the

specific, examine the motives which veer the neophyte towards the field of medicine. They can be classified under categories of public, private and psychological. The public reasons expressed are usually unoffending, ethical, and tender some worthy cause which is entirely acceptable to all concerned. They are displayed most commonly on application forms for entry into the faculty. The reasons given vary, but are similar in the effect they produce. They bear the stamp of public approval and smack of an unselfish temperament. The common themes mentioned are: opportunity for providing a useful service to the community; a curious nature directed towards the biological sciences; want of an occupation both gratifying and financially stable; and, early fascination for hospitals, operating rooms and intriguing medical accoutrement, usually expressed as, "I always wanted to be a doctor".

The private callings have more subtle spurs and they spring from the environmental setting. Commonly, they are regarded as secondary factors, which influence a decision already made. They determine the ease or difficulty the incumbent must forbear in his choice. The home is frequently the seat of these problems. For example, the grand family tree with its illustrious train of doctors is a hard link to disrupt for the youth couched in the grandeur of medicine but who has no appetite for it and, unfortunately, no courage to withstand the promptings of his parents. The economic status may be the governing factor. The lad born in penury who envisions the white collar and conservative automobile of the doctor as the ultimate in riches, must be an exceptional sort, for his incentives are trebled by the high cost of subsidizing his education. If his mettle is not strong, his expectation of a financial reimbursement for his suffering and training will be forthcoming and his practice will be one of commercial medicine. The range of these oblique conditions swing from the trifling, with application based on necessary academic achievement compounded with indifference towards other endeavours, to the tragic, where the moral pressures exerted by the family desirous of a doctor exerts its will. The considerations voiced in this group are essentially practical and of domestic colouring and being such are kept mute. The claims which paddle the student along his course, since they are bound to tradition, economy and paternal coercion, leave the obligation imposed upon him by medicine in a secondary role. He puts up with hardship to satisfy his primary motive and unless his thinking is deflected to appreciate the intrinsic quality of his studies, he will, of course, fulfil his original design: that of harvesting coins or obliging the family name with his letters.

In the psychological category, the needs of the individual *per se* are answered in order to satisfy his own integrity. These needs, which exercise considerable authority, arise from his personal life and represent his own unique method of establishing himself as a man in a society of men. The intensity and character of these deep and complex aspirations vary according to the personality as does the urgency which brings them into action. They may call forth a desire for recognition, power, independence, identity and self-assertion which, if lop-sided enough to produce a vanity or mania, can successfully thwart the labours of diligent study. For, indeed, humility and rapport in medicine preclude any use of a technical skill. The ramifications of these psychological variants are too intricate and vast to be discussed further, and are only mentioned to point to their existence.

The medical school with its tremen-

dous resources and scholarly men, does not perceptibly alter the invidious demands made upon it by the harassed freshman. It offers splendid courses in the humanities in the trial years which are followed by courses in the basic sciences of anatomy, physiology, pathology, etc. The student learns the medical vernacular and attempts to absorb and integrate the array of facts set before him, till he reaches the third and fourth medical year when he becomes an important spectator into the march of disease. He is not taught magic or wizardry, so there is no reason for him to act as a conjurer when he graduates. He is not made benevolent, invulnerable or least of all omniscient. He is briefed in the course of disease and the therapies available to stop this course. Sir William Osler summed it up well: "Medicine is a difficult art to acquire. All the college can do is to teach the student principles based upon the facts of science and give him good methods of work. These simply start him in the right direction. They do not make him a good practitioner. That is his own affair."

In a large organization, such as the University of Toronto, qualitative estimations of the personnel is unfeasible. Because of its cumbersome size, it must operate like a machine, estimating the worth of a man by some measurable achievement. The abstracts of manners, personality and sincerity which are so necessary for the art of medicine are not tested. If a student fails, he fails because he has not mastered the facts presented. He is not obliged to prove his individual fitness for the role he is going to assume. In this atmosphere where the student is relegated to a number and lectures are taught by remote control, it is easy to see how this process of fermentation can go on unchallenged until graduation day. The university may give the young doctor his letters, but it is the public which confers upon him the honours. It is the people to whom he is indebted, and until he goes out into practice and proves himself, the badge of his white coat is only one of recognition and not one of distinction.

Note: This article was not meant to crusade, teach, entertain or disparage. It is only meant to point out the obvious.

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THE PRECEPTORSHIP PROGRAM OF THE COLLEGE OF GENERAL PRACTICE

G. W. PERKIN, 5T9;
RUTH SKY, M.D.;
SALLY SAUNDERS, 5T9

THE following article was written in order to present to both the staff and the students a full picture of the preceptorship plan. Now that the first seeds have been so successfully sown, it is hoped that in the future many students will reap the numerous benefits that are to be gained from so excellent a program.

The three people who have collaborated here are: member of the original Camsi committee which proposed the plan to the College of General Practice, the chairman of the preceptorship committee of the College of General

Practice and a student who through the plan, spent two weeks with a general practitioner.

Preceptorship

Two years ago the Toronto committee of Camsi approached the College of General Practice with a proposal to reinstate one of the oldest forms of Medical Education—Preceptorship. It was felt that during our undergraduate course little contact was made with the General Practitioner and that many of the students graduating had only a vague concept of this form of Medical Practice. We felt that through the College of General Practice a voluntary programme might be established whereby students prior to entering their final year of Medicine would be able to spend a short period of time with a General Practioner.

PURPOSES OF THE PRECEPTORSHIP PLAN:

1. To provide an opportunity for the undergraduate in Medicine to observe and live with a General Practioner in his own environment.
2. To give some insight into the many various aspects of General Practice.
3. To enable the student to see disease in its earliest phase and to follow it through to its eventual resolution.
4. To provide an opportunity of seeing many of the "everyday" Medical problems seldom seen in a hospital environment.
5. To enable the student personally to come in contact with the doctor-family relationship.
6. To create a greater awareness of the social, economic and religious aspects which are such an important part of Medical Practice.
7. To provide a brief exposure to office management.
8. To provide the doctor with stimulation for further study and to satisfy his desire to pass on knowledge and experience to others.

Objectively the Plan to date appears to have met all these purposes and it is hoped that each year more students will avail themselves of this opportunity.

—G. W. Perkin

The Preceptorship Programme as seen by the Preceptors

The College of General Practice is endeavouring to contribute to the knowledge of medical students. With the preceptorship programme, we demonstrate the manner in which the family physician serves his patients in the community.

We have received wonderful letters from the physicians who participated in 1958. The plan was enthusiastically endorsed by all the doctors, and they unanimously complimented their students on good manners, intelligence, and keen interest.

The student was treated as a visiting young colleague. He was introduced to the patient, and then sat quietly by as the doctor carried on with his work. Many spirited discussions ensued between house calls and office visits, and carried on in the physician's home after the day's work was done. Many of the preceptors mentioned the satisfaction of organizing thoughts in an orderly fashion to explain the conclusion reached.

Many of the students spent some time with more than one doctor. Most physicians work with one or more colleagues in an arrangement whereby one is on call for specified days or week-ends. In this manner, the preceptorship programme demonstrates the friendly cooperation among doctors, as well as some variation in techniques of talking with patients. Another important relationship the students observed, was that of the general practitioner to the specialist. The students saw some types of illnesses

which were referred, and saw the role of the family doctor in such a situation.

The actual mechanics of managing an office interested all the students. They became aware of the importance of an intelligent receptionist, an answering service, and accurate bookkeeping records.

The general impression of the College of General Practice is that the preceptorship programme is a success. We believe that it is a progressive step in clinical teaching, whether the student chooses a career of general practice or any specialty.

—Ruth Sky, M.D.
Chairman of the
Preceptorship Committee

The Preceptorship Programme as seen by the Student

While in medical school most students are far too busy learning facts to remember that a medical practice of any sort deals with people. Along with this many have rather forgotten why they originally undertook the study of medicine. Being in this state myself, I was pleased when the members of my class were offered the chance to take part in the preceptorship plan. I accepted, not because I was particularly interested in general practice, but because it gave me a chance to see how a medical practitioner lived.

For two weeks I quite literally shadowed my preceptor—going on house calls, to the hospital, to the office, eavesdropping while advice was given over the telephone, getting up at 5:30 a.m. to watch a baby be delivered.

It took only a few hours to get completely orientated in the art of medicine again. Suddenly it was the people who were important. A person came to the doctor to ask how he could feel better. The doctor then used the facts he had learned in medical school to discover why the patient was not feeling well, but in replying, he talked to the person and not the disease. This is the essence of what I learned during my stay. Patients are people and not just a case of pneumonia as they are so apt to become on the ward.

Insidiously, the fact that I was enjoying general practice more than anything I had ever done came to the surface of my thoughts. Watching the doctor deliver a woman's third child, and then a week later watching the woman's husband bring the oldest child in for a pre-school examination, made me realize that general practice has a very pleasant continuity. It also is a challenging occupation, for it is up to the family doctor who first sees the patient, to recognize any abnormality with which the person may present.

My preceptor, like all the others about which I have heard, was more than willing to answer all my questions about the mechanics of setting up and continuing a practice. This alone is invaluable, since there are many of us who otherwise would have absolutely no idea of how to begin. By the sharing of night calls and weekends with a colleague, I found that it was possible to have an interesting and full practice but also to be able to participate in some personal activities. This is an important consideration for anyone who does not want to practice medical heroics, but at the same time is interested in a general practice.

As a result of these two weeks I feel that not only have I gained a friend and learned how interesting it is to be a family doctor, but more important I have discovered the art of medicine. For this last reason if no other it is worthwhile for any student to participate in the preceptorship plan. Those who do will undoubtedly find that they have gained more than they believed possible, even to the extent of being converted to general practice!

—Sally Saunders

A PRECEPTORSHIP IN A SMALL TOWN

L. F. W. LOACH, 5T9

APPROXIMATELY sixty miles east of Peterborough and twenty-five miles north of Belleville in moderately wooded and rolling countryside lies the small town of Tweed. Through the outlying farms and past the town itself flows a small river which at the southern end of Tweed widens out into a small lake. During the summer months this lake attracts between 1,000 to 1,200 tourists who augment the usual population of 1,600. These part-time inhabitants fatten the town's income besides providing added medical work. In the fall, deer and duck hunters find the game abundant. Revenue comes mainly through farm produce, the Nichol's Chemical Company (grossing about a quarter of a million dollars annually), a veneer wood factory and a fabricating steel plant besides local merchants. Materials and food cost the same as in larger cities but the cost of labour is at a much lower level, a skilled labourer making between $1.20 to $1.40 per hour, as against $2.10 to $2.25 for similar work in Toronto. Most of the workers and townspeople are in the older age groups because young persons find jobs at home hard to get and consequently move away. This has a definite influence on the medical problems seen. There are two public schools and a small high school.

Dr. G. Gibson Allen, 33, from Ottawa is a McGill graduate of 1950 who, after his junior interne year entered a surgical postgraduate course. However he subsequently entered general practice. Married, father of two girls 5 and 6, he lives with his family in an attractive eight-room house. Dr. R. Stanley Berry, 31, also from Ottawa, is a McGill graduate of 1952. After his junior interne year he spent 2 years in Port Colborne with a general practitioner. Returning to Ottawa, he studied general surgery for a year and then entered general practice in partnership with Dr. Allen. He too is married, and the father of four young children, and has recently moved into a modern seven-room home on two acres of wooded property. Besides their office practice, both men are on the active staff of Belleville General Hospital where they have surgical privileges, are coroners for Hastings County and are members of the College of General Practice. To quote Dr. Allen, "We like to feel we are in general practice through choice rather than through necessity".

Using the office of a retired doctor as their headquarters, Drs. Allen and Berry operate a thriving practice of roughly 20,000 patient visits annually. Their territory covers 1,200 square miles and because of this vast area, they encourage office calls by charging fifty cents a mile one way. Ninety-five per cent of their visits are office calls.

The waiting room of the offices opens separately into private consulting rooms. These in turn open into a dispensary which is equipped to supply all commonly used drugs and preparations. The dispensary leads to the treatment room at the back of the house which contains a bed, autoclave, emergency surgery apparatus, X-ray, and both therapeutic and diagnostic lab equipment. X-rays are are developed in a basement darkroom. Soon these facilities will be enhanced by a small ECG unit. On the second floor are the two-room offices of an optometrist who sees patients from the Tweed area on Tuesdays. The doctors employ a graduate nurse to assist with therapy, to maintain instruments and materials and to deal with the endless paper work of modern

medical practice; and a chartered accountant to keep the files in order and handle the complexities of tax problems and bookkeeping. The business grosses about $60,000 annually; the overhead is $30,000; personal taxes and insurance require $14,000, leaving a net of $8,000 each on which each doctor lives comfortably in his rural setting.

An average day starts with breakfast at 7:30. At 7:45 the 25-mile trip to Belleville starts. Rounds consume about an hour after which either or both doctors conduct or assist at operations. Then back to Tweed for morning visits, although there are no formal morning office hours. Lunch is between 12 and 1. Afternoon hours are posted as from 2 to 4, but both doctors work regularly from 1 to 5. Dinner from 5 to 6. There is a steady stream of patients from 7 until 9:30. Each man works every other night and every other Sunday. A switchboard transfers calls during off-hours to either doctor's home. Wednesday afternoon is a holiday but this usually only proves theoretical.

Impressions, following a two-week preceptorship:

1. Working with these two men provided opportunity to compare the theory of medical teaching and the practical routine of a large city hospital (as in Toronto) with the routine of small town G.P.'s in the office; the intuitive quality of office examination was evident.

2. The paper work, bookkeeping and red tape of health and insurance schemes was impressive. Helpful hints about setting up books, contacting a chartered accountant and dealing with insurance claims resulted.

3. The chance to observe the across-the-office desk rapport was gratifying.

4. Many incidentals not taught in medical school were learned, for example, setting up an equipped office, an office dispensary, and what to look for when choosing a site for an office.

5. Although only in Tweed for 2 weeks, the writer was able to observe that many conditions considered rare by undergraduates were not so rare in practice.

6. There were times during the day when things dragged a little, but this was more than balanced by the hospitality, friendship and thoughtfulness of the doctors and their wives.

7. The writer would recommend to any other undergraduates considering general practice (and also to prospective specialists) the opportunity of taking a preceptorship. It provides a thoughtful contrast to school medicine, and an invaluable opportunity to learn how established doctors have succeeded and what their experience has taught them, as well as a pleasant vacation with people who are interested both in young medical people and the age-old profession of medicine.

HEART DISEASE IN PREGNANCY

PAUL E. A. HISCOX, 5T9

APPROXIMATELY one per cent of pregnant women have signs, or at least a history, of heart disease. Of these cases, rheumatic heart disease occurs in over ninety per cent. The commonest lesions are of the mitral valve, particularly stenosis. Aortic insufficiency, sometimes coupled with mitral stenosis, is the next most frequent lesion. Congenital heart disease, particularly atrial septal defect, accounts for about two per cent of cases and the remaining five per cent

is due to hypertensive, thyrotoxic, arteriosclerotic and syphilitic disease. Heart disease is an important cause of maternal mortality, ranking fourth behind haemorrhage, toxaemia and infection.

Physiological Changes Causing Increased Burden on the Heart in Pregnancy

There are, of course, many such changes which occur. However, the most important ones which may predispose to the development of heart failure are:—

1. Increase in total blood volume (both fluid and cellular elements) by about thirty-five per cent. The blood volume begins to increase about the tenth week of pregnancy and reaches a peak between the twenty-ninth and thirty-third weeks. As term approaches, the blood volume gradually diminishes but does not reach normal level until about two weeks post partum. Around twelve hours after delivery, the blood volume increases again temporarily, but soon returns to its reducing way. The increased circulating volume naturally requires the heart to work harder. Consequently, if the heart is diseased, and incapable of handling this extra burden, failure will occur, particularly between twenty-nine and thirty-three weeks, or twelve hours post partum.

2. Cardiac output is increased. This is due to both the increased blood volume, and the increasing heat rate. In mitral stenosis, the blood must flow more rapidly through the damaged valve, to maintain the cardiac output, since the size of the flowing blood column is diminished by valvular narrowing. A more rapid flow is effected by a rise in pressure in the left atrium, as a result of greater filling of this chamber.

3. The patient's body weight and basal metabolic rate are both increased. A weight gain of about twenty pounds occurs due to fluid retention plus the foetal weight. These changes cause the heart to function more forcibly. The growing foetus and enlarging maternal reproductive organs require ever-increasing amounts of oxygen. As a result there is a progressive rise in maternal oxygen consumption, reaching a peak about fifteen per cent above normal in the last month of pregnancy.

The diagnosis of heart disease or cardiac failure in pregnancy is often difficult. This is due to several factors. The retention of a certain amount of body fluid is normal in pregnancy. Thus, to determine whether or not the patient's oedema is due to cardiac failure is sometimes difficult. If there are, or have been, any heart murmurs present, these may be changed due to the increased cardiac output and blood volume. The displacement of the heart upwards, forwards, and to the left, by the growing pregnant uterus, may be confused with cardiac enlargement and hypertrophy due to congestive failure. For these reasons, any investigation should be done as early as possible in pregnancy, since diagnosis at this time is easier, more accurate and more important.

Cardiac patients may be classified according to the criteria set forth by the New York Heart Association as follows:—

Class I. Patients with cardiac disease and no limitations of physical activity. Ordinary activity causes no discomfort, and these patients do not suffer from angina pectoris or other symptoms of cardiac insufficiency.

Class II. Patients with heart disease and slight limitation of physical activity. They are comfortable at rest, but undue fatigue, palpitation, dyspnoea, or angina, are produced by ordinary activity.

Class III. Cardiac patients with marked limitation of physical activity. Less than normal activity produces angina and other symptoms, although these patients are comfortable at rest.

Class IV. Members of this group are unable to carry out any physical activity without having discomfort. Even at rest they have symptoms of cardiac insufficiency.

Other factors to be considered in evaluating the extent of heart disease in the pregnant patient and the possibility of the development of cardiac failure are:—

(a) The patient's age—cardiac failure occurs more often in patients over thirty-five years of age.

(b) The duration of the heart disease—the longer it has been present the greater the extent, and the greater the chance of the development of failure.

(c) A history of previous heart failure, particularly if it occurred early in pregnancy, since it is almost certain to become more severe later in the pregnancy. If a patient had cardiac failure in a previous pregnancy, she is very likely to have failure in a subsequent pregnancy. The degree of parity is not very important.

Although a patient may have had a past history of one or more normal deliveries without the development of cardiac failure, this does not necessarily indicate that her present, or any future pregnancy, will go uncomplicated. The pregnant cardiac patient may fail at any time!

Management of the Pregnant Cardiac Patient

1. prenatal

The primary concern in prenatal care is prevention of cardiac failure. It is advisable to have the close co-operation of a cardiologist throughout the duration of pregnancy.

(a) Frequent examinations are important. The patient should visit her doctor every two weeks, more often if indicated, and weekly after the sixth month. It is less important (at least to the patient) and certainly less disastrous, to diagnose mitral stenosis when the lesion really is not present, than to miss the diagnosis when it actually does exist. One could not be criticized nearly as much for the former mistakes as for the latter. Because most patients are normal, the physician's examination may become cursory, and an important diagnosis may be missed through his inattention.

(b) The patient should be advised to avoid any emotional stress and strenuous activity, for her heart cannot withstand this as well as can a normal one.

(c) She should have twelve hours of rest per day, including at least two hours more sleep per night than usual. From the twenty-ninth to thirty-third weeks, or if her exercise tolerance is low, the patient should have even more rest per day.

(d) Her weight should be carefully controlled by restricting both calories and sodium in her diet. Diuretics may be used if excessive fluid retention occurs.

(e) Any infection, no matter how slight it may seem, must be treated promptly and adequately. Even a common cold merits bed rest and prophylactic antibiotics.

(f) All pregnant patients should receive iron therapy. This is particularly important in cardiac patients, since the development of anaemia may eventually lead to cardiac failure.

(g) The patient should be admitted to hospital for rest, at least one week before term. Of course, if any symptoms or signs such as increased shortness of breath, severe oedema or marked tachycardia should develop before this last week, she should be hospitalized at once and appropriate treatment should be administered immediately.

2. during labour and delivery

Every effort should be made to make these two aspects of pregnancy as easy

as possible on the patient. A little more sedation than usual should be used in the first stage of labour (avoiding hyoscine because of its possible excitatory effects). In order to shorten the second stage of labour and thereby lessen the strain on the heart, forceps delivery is done. In case of emergency, it is best that the anaesthetist for the delivery be a specialist in this field. Cyclopropane and ether are the safest and most commonly used inhalent anaesthetics for a cardiac patient. Pudendal nerve block is also satisfactory. Spinal and epidural anaesthesia are avoided because of the tendency for these to produce a fall in blood pressure. Because of the danger of anoxia, nitrous oxide alone is best avoided.

Vaginal delivery is preferred to caesarian section in these patients. Indeed, the latter should be resorted to only for purely obstetrical reasons, e.g. severe cephalo-pelvic disproportion. Guttmacher suggests that the danger in caesarian section is probably the sudden addition to the general circulation of all the blood in the uterine vessels due to the sudden contraction of the uterus after section.

The incidence of post-partum haemorrhage is slightly higher in patients with heart disease. Since this is a real emergency in cardiac patients, meticulous care must be exercised to avoid it.

3. AFTER DELIVERY

More rest than usual is required, and the patient should be watched closely during the first few days after delivery for the development of heart failure. She should be kept in hospital for at least ten days, and ambulation should be delayed somewhat longer than normally. Cardiac mothers may be permitted to nurse their babies, since only in severe heart disease are the circulatory demands relatively increased by lactation to the point of being harmful to the patient's condition.

INTERRUPTION AND TERMINATION OF PREGNANCY

There are now very few indications for the termination of pregnancy. These indications are to some extent controversial, and each case must be carefully assessed on its own merits.

If heart failure occurs early in pregnancy, i.e. before the twenty-fourth week, therapeutic abortion should be considered. If it occurs later, this procedure should not be followed since the strain of the pregnancy on the patient will be less than the operative termination. If the patient can be safely carried over the period of maximum increase in blood volume, i.e. twenty-nine to thirty-three weeks, no interruption need be performed since this volume decreases thereafter.

Pregnancies that are terminated are those of patients in classes III and IV. Sterilization by tubal ligation is sometimes considered after the second successful pregnancy in these same patients.

The advisability of subsequent pregnancy depends on various factors. If heart failure or diminished exercise tolerance has occurred, future pregnancy is best avoided. If advice on contraceptive methods is unlikely to be followed (by patients with low I.Q.), then sterilization should be recommended. Religious and socio-economic factors and the possible impairment of the patient's ability to look after her family are important to consider when determining whether or not the patient should become pregnant again.

If future pregnancies are thought to be safe, there is no point in the patient's waiting for a long time before becoming pregnant. Her heart disease will not improve in time. On the contrary, it will more likely worsen to some extent. This, of course, pertends to those types of

heart disease not amenable to surgery. Valvulotomy, particularly mitral commissurotomy may be done early in the pregnancy of suitable patients.

The maternal mortality rate in pregnant cardiac patients is about two per cent. A higher foetal mortality rate exists due to prematurity, since these patients often enter premature labour.

In almost all cases of pregnancy occurring in a woman with heart disease, the patient can pass through the pregnancy safely and productively. With the cooperation of the patient and the persuasiveness of a physician who understands the basic haemodynamics underlying the condition, pregnancy in a cardiac patient has an excellent chance of being completely successful.

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THE TREATMENT OF HYPERTHYROIDISM WITH RADIOIODINE

H. P. JAMES, 5T9

THE thyroid gland produces thyroxine, a hormone which is necessary for the normal growth and development of the body as well as for the maintenance of normal metabolism.

The value of stable iodine in the treatment of thyroid disease has been known clinically for many years. Since the days of Hippocrates, burnt seaweed or sponge, both of which are rich in iodine, have been used to treat goitre. It is now known that in the so-called "goitre districts", the iodine content of the soil, water and air is very low. These areas are also far from the sea—the Alps, Himalayas, the peak district of Derbyshire in England, and in parts of North America, one being this part of Ontario. In 1821 Coindet reported the use of the element iodine in the treatment of goitre but in 1868 Trousseau believed that iodine as a rule aggravated hyperthyroidism. In 1923 Plummer pointed out the value of iodine in the preparation of hyperthyroid patients for a surgical thyroidectomy.

In more recent years the role of stable iodine in thyroid function has been more fully evaluated. Iodine is reduced to iodide and absorbed by the G.I. tract—mostly by the small intestine. The thyroid gland selectively concentrates a portion of this iodide to form thyroid hormone. Once formed, thyroxine may be stored as thyroglobulin in the follicles of the gland. Thyroglobulin is converted to the active hormone thyroxine which is released into the blood stream. The uptake of iodine and the rate of formation and release of thyroxine are regulated by the thyroid stimulatory hormone of the Anterior Pituitary gland, which is released when the blood level of thyroxine is lowered.

Because the body, including the thyroid gland, is unable to distinguish between stable and unstable radioactive iodine, Radioiodine began to be used for diagnosis and therapy in 1941 by Chapman. In diagnosis a small dose of Radioiodine is given by mouth and the percentage uptake of Radioiodine is calculated from the measurement of the amount of radiation present over the thyroid 24–48 hours later, taking into account the half-life of the Radioiodine. This is a more direct test than the Basal Metabolic Rate but not quite as good as

the properly done Protein Bound Iodine Test. Both the Radioiodine uptake and the Protein Bound Iodine determinations are unreliable if iodine containing medications such as Lugol's solution, cough syrups, or dyes containing iodine for X-ray purposes, have been used shortly before testing. The Basal Metabolic Rate test measures oxygen consumption and hence is an index of the peripheral effect of thyroxine. It is readily altered by excitement, apprehension, lack of sleep and many other subjective factors which cannot be well controlled.

In treating hyperthyroidism two facts make Radioiodine useful:

1. The thyroid has a natural avidity for collecting iodine, both stable and radioactive.
2. Within the thyroid the Radioiodine disintegrates and emits gamma rays and beta particles which penetrate into and destroy thyroid tissue.

The dosage of Radioiodine to be given depends on at least six factors:

1. The weight of the gland.
2. The type of gland, i.e., diffuse hyperplastic or multinodular gland.
3. The amount of Radioiodine which enters the gland.
4. The actual amount of radiation which is emitted in the gland.
5. The sensitivity of the thyroid cells to radiation.
6. The biological turnover rate of Radioiodine in the gland.

The recommended average dose is 160 microcuries of Radioiodine per gram of estimated thyroid weight.

Radioiodine should only be given under certain circumstances. It should never be given to pregnant women, since after the 19th week the foetal thyroid will take up Radioiodine. It is unwise to give Radioiodine to children with hyperthyroidism because of the high recurrence rate of the disease in this age group. There are certain remote dangers such as sterility, mutation of genes and carcinoma due to radiation. However, none of these dangers has yet been recognized after treatment with Radioiodine. Therefore, Radioiodine should be used in treating hyperthyroidism in any patient over the age of twenty who is not pregnant.

Course after Treatment

A favourable response to Radioiodine is based on three criteria:

1. Disappearance of hyperthyroid symptoms.
2. Appreciable decrease in size of the gland.
3. Persistent fall in indices of thyroid function.

There is as a rule little or no change noticed in the patient for two to three weeks, in fact there might be an exacerbation of symptoms due to sudden release of stored thyroid hormone already present in the gland. Then the patient gradually improves and many patients return to normal in three months.

The majority of patients are euthyroid four months after treatment, and a second dose should not be considered until this time. However, some patients take six months and longer to return to the euthyroid state, so as long as the patient continues to improve and the indices of thyroid function decline, no further dose should be given.

Efficiency

Results of treatment with Radioiodine in 520 patients with hyperthyroidism show:[1]

Responded to 1 dose	391
Responded to 2 doses	51
Responded to 3 doses	9
Responded to 4 doses	2
Better but toxic	32
Died	35

Of the thirty-two patients classified as better but toxic, five were operated on and improved, eight had two doses of

radiation and four had three doses. These patients improved but their indices of function are still above normal. The remaining fifteen patients have improved somewhat after a single dose, and either persisted with high indices of function or have not had adequate follow-up. Of the thirty-five who died at varying intervals after treatment, sixteen had responded and died of diseases not related to the thyroid between four months and seven years after treatment. Sixteen others died four months or less after treatment before the full effect of their radiation therapy could be assessed, and none of diseases related to the thyroid. The final three of the thirty-five died after one or two doses, but of diseases not related to the thyroid.

Complications

The complications of treatment with Radioiodine are relatively minor in comparison with those of other types of treatment. Some patients have an exacerbation of their hyperthyroid symptoms during the first three weeks after Radioiodine administration. Five per cent of patients develop thyroiditis, with a painful tender thyroid gland, pain on swallowing and referred pain to the ears, beginning in second week after Radioiodine administration and lasting for two to three days. Temporary or permanent myxedema occurs in 15% of patients treated with Radioiodine but these patients can be well controlled on a maintenance dose of 2–3 gr. dessicated thyroid per day, and this is not considered a serious complication.

Summary

(1) For many years it has been known that iodine is taken up by the thyroid gland to form thyroxine.
(2) The thyroid gland does not differentiate Stable Iodine from Radioactive Iodine, and readily takes up I^{131} which destroys thyroid tissue.
(3) In hyperthyroidism an estimated amount of thyroid tissue can be destroyed by administration of a single dose of Radioiodine. The amount to be given depends on several factors, e.g., type, size and sensitivity of gland to Radioiodine, and the biologic half-life of Radioiodine in the gland. At present only non-pregnant patients over 20 years old are treated with Radioiodine.
(4) The majority of hyperthyroid patients are improved after one dose of Radioiodine, and most have returned to normal four months after treatment.

Complications occasionally follow treatment with Radioiodine and include: exacerbation of symptoms, thyroiditis, temporary or permanent myxedema.

However, due to the large percentage of good results and the small number of relatively minor complications Radioiodine administration is the treatment of choice in non-pregnant adult patients with hyperthyroidism.

Acknowledgement

I would like to thank Dr. M. W. Johnston for his help in preparing this article.

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CASE REPORT

J. T. SHEPHERD, 5T9

MR. G. G., a 59-year-old miner was admitted to Copper Cliff Hospital on February 9, 1958, complaining of loss of appetite, increasing weakness and fatigue, and shortness of breath on exertion for one month, as well as discomfort

in his lower anterior chest and epigastrium for about two weeks.

History of Present Illness:

This man was well until approximately December 20, 1957, when he developed a cold associated with fever, malaise, and a cough productive of a small amount of sputum which was clear of blood. He remained essentially the same until January 22, 1958, when he developed a sharp knife-like pain in the left axillary region which was aggravated by deep inspiration. He was treated with penicillin and syrup of codeine, with the disappearance of his axillary pain and improvement of his general condition. However, on physical examination at this time, the trachea was found to be shifted to the right and there was dullness to percussion and marked diminution of breath sounds over the left lower lobe. He was referred to the hospital for investigation of these findings.

History of Past Health:

The patient had worked as a miner for 29 years and had enjoyed fairly good health. He smoked 10–20 cigarettes per day. He was hospitalized in September, 1957, and underwent a right nephrectomy for pyelonephritis and multiple calculi. A chest X-ray taken at that time was entirely negative. He had had no previous history of chest disease.

Physical Examination:

The patient was pale and looked chronically ill, but showed no evidence of recent weight loss. He was well nourished and well developed. His trachea was shifted slightly to the right and there was a flat percussion note and absence of breath sounds over the lower two-thirds of the left chest. The upper third of the left chest and the right chest were clear. There were no adventitious sounds heard. The heart sounds were distant but there were no other cardiovascular findings. The B.P. was 130/80. There was no lymphadenopathy.

Investigations:

Urinalysis: negative; *Hb.*: 70%; *differential*: normal; *smear*: hypochromic, normocytic. *Chest X-ray*: there was a density in the left apical region and a fluid level in the left pleural space extending as high as the fourth interspace anteriorly. There was also collapse of the ninth dorsal vertebra. *Thoracentesis*: 260 cc. of grossly bloody fluid were removed and sent to the provincial lab for cytological examination which proved negative for malignant cells. *Sputum*: Normal respiratory flora only were found.

Differential Diagnosis:

1. Carcinoma of the left lung parenchyma with involvement of the pleura.
2. Possible primary carcinoma in the left pleura.

Subsequent Course:

The patient remained in hospital until March 13. During this period five thoracenteses were done and a total of about 8,000 cc. of almost pure blood were removed. The patient also received 8 bottles of whole blood, as his Hb. level fell continuously, being as low as 43% on one occasion. It was 70% on discharge. Cytological examination of all fluid removed from the left chest failed to reveal any malignant cells and repeated sputum examinations were negative. During this period the density in the left apex was observed to have increased 2–3 times in size.

On March 13, the patient was transferred to the Toronto General Hospital for further investigation and treatment. Here a further 4,000 cc. of bloody fluid

were removed from his chest and he received four bottles of blood. Chest X-rays showed a further increase in the size of the density in the left apex. As a result of this a left thoracotomy was carried out. This showed the pleural space to be largely obliterated with adhesions, but able to be opened by careful digital manipulation. Pleural nodules could be felt in the left anterior axillary line. One of these was removed for pathological examination. Further exploration of the pleural space was not deemed advisable, the thoracotomy incision was closed and the patient made an uneventful recovery.

He subsequently received radiation therapy of a total of 2,000 roentgens to his left anterior chest and 2,000 r. to his left posterior chest in doses of 500 r. over a period of 26 days. He received three more bottles of blood. He was discharged on April 26, feeling fairly well and with a Hb. of 73%.

He was seen in the O.P.D. on May 2, at which time he felt and looked well. His chest was clear and there was no lymphadenopathy.

He was seen again on May 30, complaining of periodic pain in his left axillary region. Examination of his left chest showed diminished breath sounds in his left axillary region and left base, as well as rales in the left base.

He returned on June 30 having noticed streaking of blood in his sputum for several days. He also complained of loss of appetite and increasing weakness. His left lower chest was dull to percussion and breath sounds were decreased. A chest X-ray showed some fluid, increased density throughout the lung, and increased pleural thickening.

He was readmitted on July 6 appearing very ill, in considerable distress and very weak. He was orthopnoeic and unable to rest except on his left side. He was having severe bouts of coughing and hemoptysis. His whole left chest was dull to percussion anteriorly and breath sounds were absent. He was suffering a good deal of pain. His Hb. was 25% and the smear showed markedly hypochromic red blood cells. He was given three bottles of blood over the next few days, but expired on July 10.

Autopsy Findings:

(a) *Gross Examination*: The left pleura was completely obliterated by tumor from 0.5–2.0 cm. thick. The tumor was white and tough with numerous spaces from 1–15 mm. in diameter filled with blood. It formed a thick coating over the lung but did not seem to invade it. It was densely adherent to the intercostal muscles.

Metastatic tumor was found in: (1) the left internal mammary chain of lymph nodes which were of the size of a split pea, with all members of the chain being hemorrhagic; (2) the left para-aortic nodes at the level of the kidney, where lobular white growth could be seen.

(b) *Microscopic Examination*: The tumour resembled closely a loose-textured fibrosarcoma but showed a definite tendency to form blood filled spaces and "villi". The cells were of medium size and generally elongated. The nuclei were relatively large, mostly round and vesicular, and had well-marked nucleoli. Mitoses were scanty. There had been some invasion of the peripheral alveoli of the lung, the adventitia of the left branch of the pulmonary artery and the left hilar nodes, as well as those sites noted on gross examination.

Diagnosis:

Hemangioendothelioma of the pleura.

Acknowledgement

The author wishes to express his thanks to Dr. M. J. B. Stalker and the Copper Cliff Hospital for much of the material contained in this report.

ABSTRACTS

Relationship Between Cancer and Viruses. Wendell M. Stanley. A.M.A. Archives of Internal Medicine. 102:939, 1958.

Experimental work has proven that there is a direct relationship between viruses and cancer in animals. This was first noted in 1911 when Peyton Rous found that sarcoma could be passed in chickens with cell free filtrates. Later work on rabbit tumors suggested that chemical carcinogens cause cancer by working through viruses already present in the cell. The Bittner mouse factor has indicated that there is an interplay between viral, genetic, and hormonal factors about which very little is known.

So far there has been very little work on viruses and human cancer. However the growth of viruses in human tissue cultures promises to be a powerful experimental approach. The cytopathogenic effect on HeLa cells by the APC virus is an example of this.

It can be postulated that carcinogens produce cancer by causing mutation of a latent virus in the cell. In some cases viruses seem to grow only in cells at the time of cell division much like the DNA of the genes.

The finding of abnormal particles in certain filtrates of human cancer is stimulating research on the relationship between viruses and human cancer.

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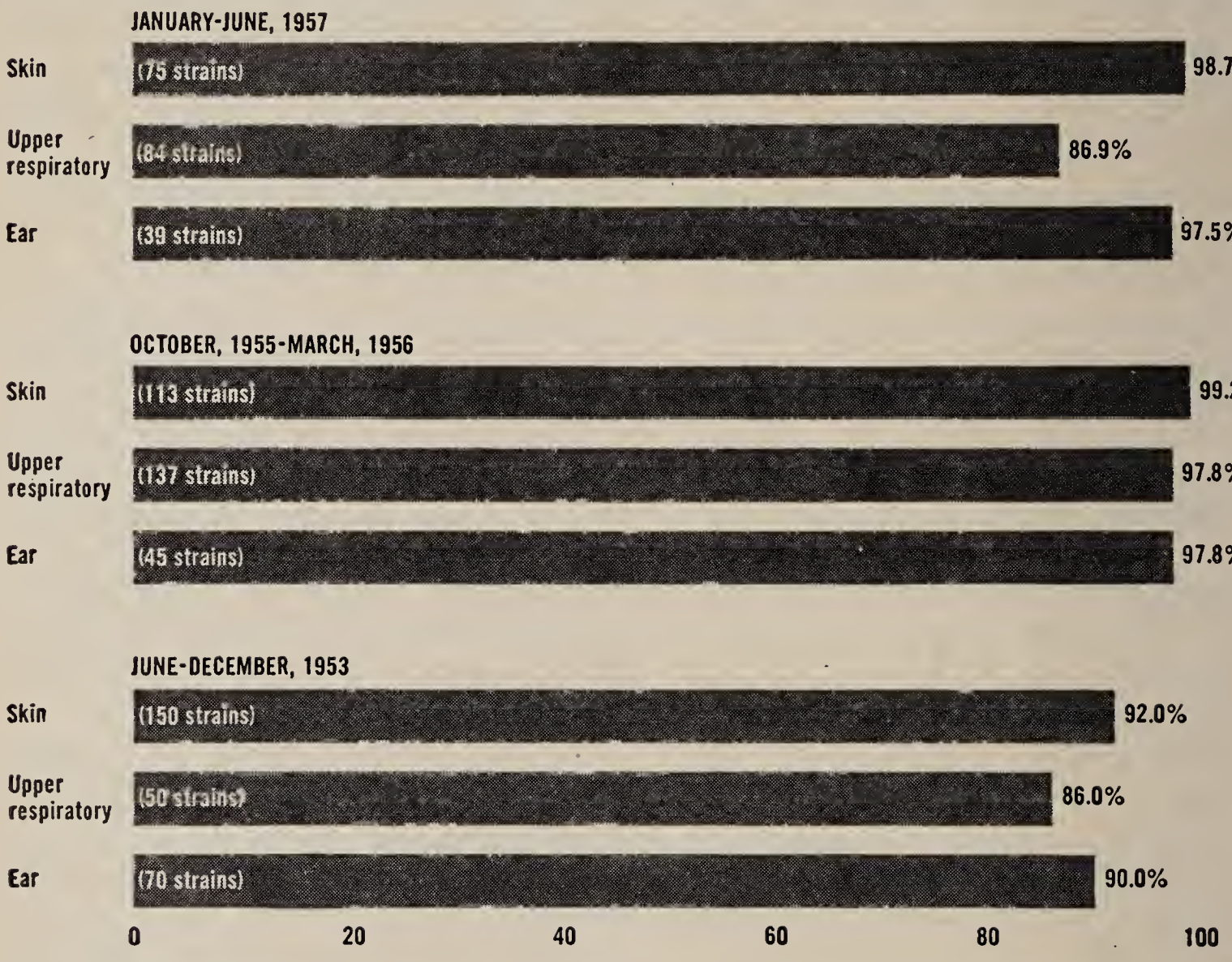

*Adapted from Royer, A., in Welch, H., & Martí-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 783.

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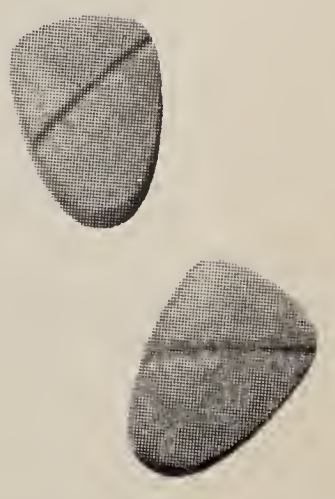

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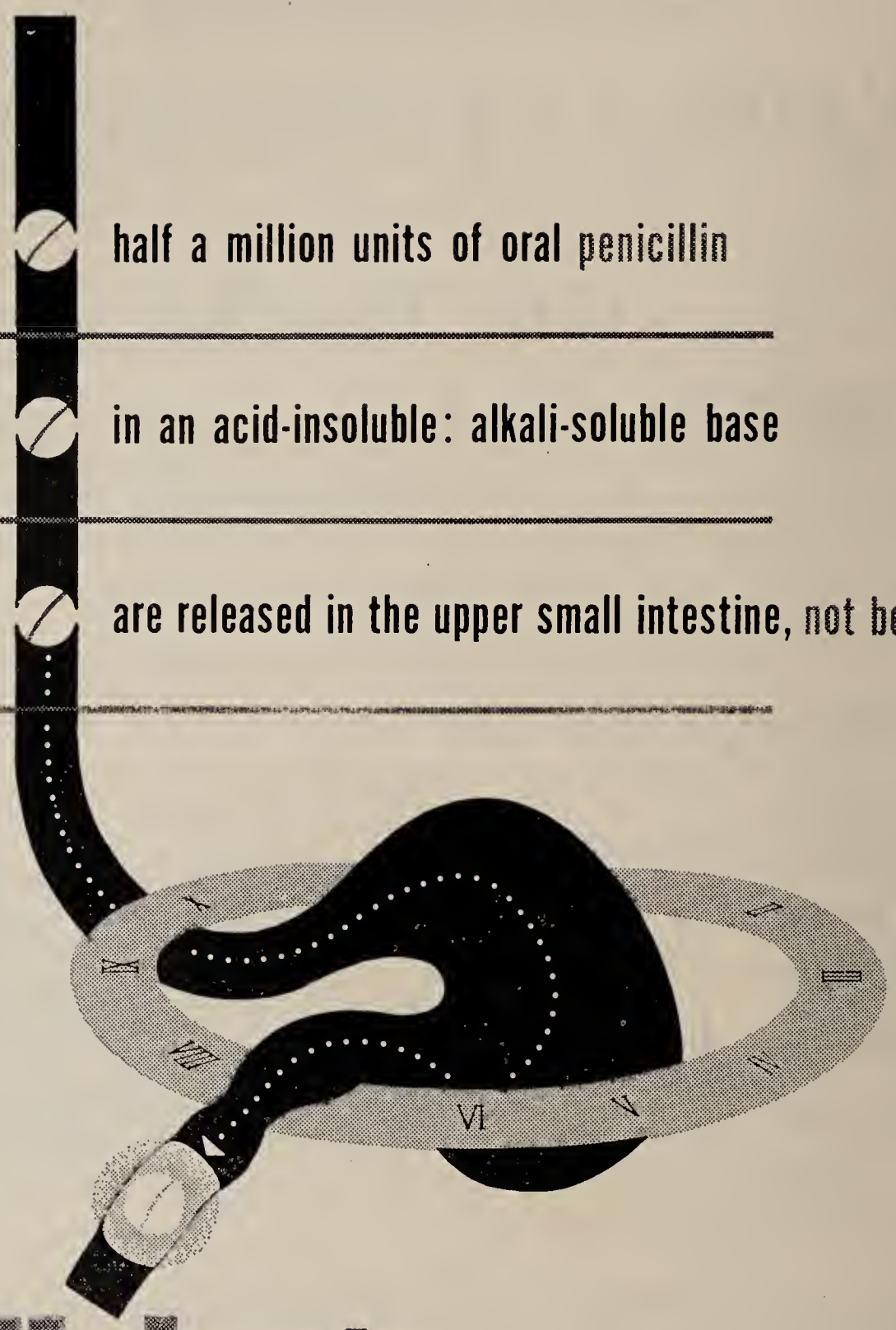

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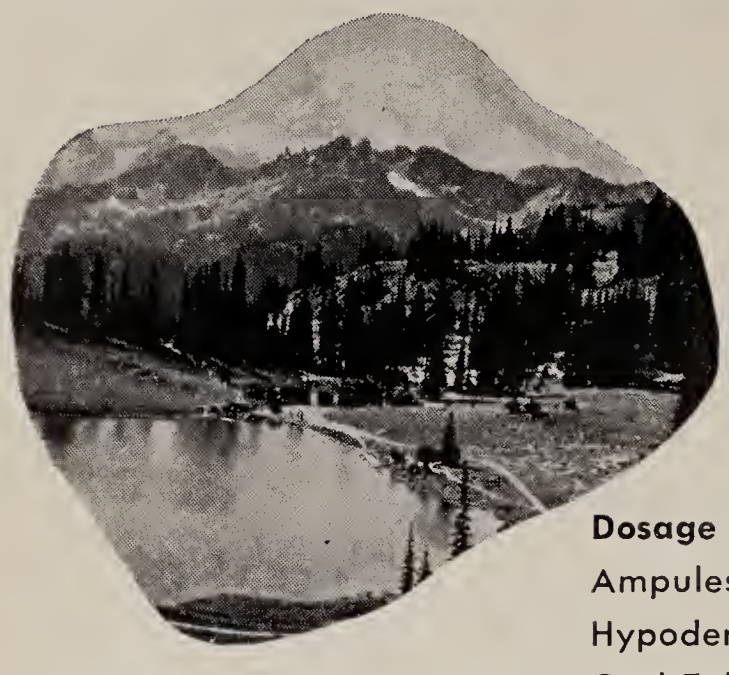

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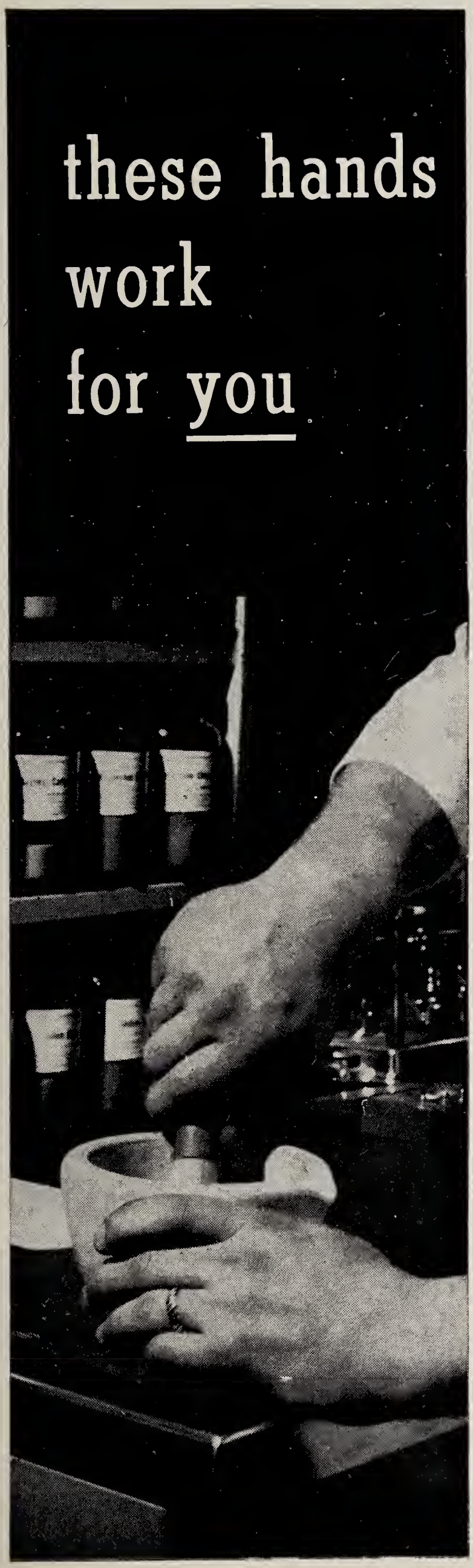

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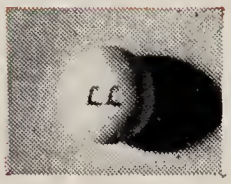
every  antibiotic

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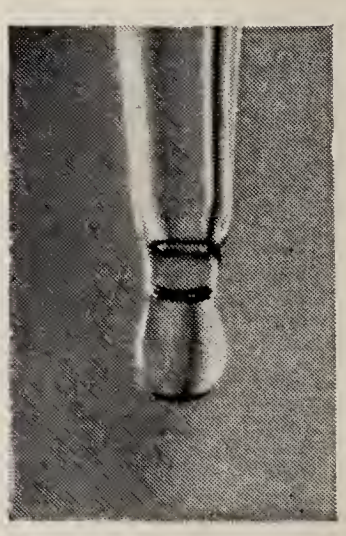

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